CYTOLOGICAL EVALUATION OF SALIVARY GLAND LESIONS WITH CATEGORIZATION USING THE MILAN REPORTING SYSTEM

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ABSTRACT

Introduction: Salivary gland neoplasm comprise nearly 6.5% of all the lesions sampled in the head and neck, amongst these, nearly 40% are malignant. Fine needle aspiration cytology is a highly reliable technique for preoperative diagnosis of salivary gland lesions and has garnered widespread use and acceptance among clinicians and their patients.

Aim: To study the detailed cytomorphological features of all salivary gland lesions and categorize them according to the Milan system for reporting salivary gland lesions.

Materials & Methods: Fine needle aspiration smears from salivary gland lesions were received in the Department of Pathology of Dayanand Medical College and Hospital, Ludhiana over a period of five years of which three and a half years was done retrospectively and one and half years prospectively and (1st July 2015 – 30th June 2020).

Results: A total of 160 cases were analysed with slight male predominance (M:F ratio -1.1:1). Swelling (96.9%) was the most common clinical presentation. Parotid gland (68.1%) formed the most frequent gland aspirated. Cytological smears were categorized according to Milan system of reporting salivary gland cytopathology as Non Diagnostic (4.4%), Non Neoplastic (38.8%), Atypia of undetermined significance (9.4%), Suspicious for malignancy (1.2%) and Malignant (4.4%). Neoplastic category in our study comprised of the most number of cases (41.8%) and was further subcategorized into Benign (35.6%) and salivary gland neoplasm of uncertain malignant potential (6.2%). The risk of malignancy for each category were non neoplastic-14.2%; Atypia of undetermined significance-11.1%; Neoplastic, Benign 11.6%; Neoplastic, SUMP-0%; Suspicious for malignancy- 50%; Malignant- 100%.

Conclusion: Milan system helped us categorize the salivary gland aspirates into distinct diagnostic categories. Thus the risk of malignancy could be estimated.

Keywords: Salivary gland, Milan system, Risk of malignancy, parotid gland.

ABBREVIATIONS

AdCC	Adenoid cystic carcinoma
ASC	American society of cytopathologist
AUS	Atypia of undetermined significance
BCA	Basal cell adenoma
FNA	Fine needle aspiration
FNAC	Fine needle aspiration cytology
LESA	Lymphoepithelial sialadenitis
MEC	Mucoepidermoid carcinoma
MSRSGC	Milan system for reporting salivary gland cytopathology
NA	Not applicable
N:C	Nuclear cytoplasmic ratio
PA	Pleomorphic adenoma
PPV	Positive predictive value
ROM	Risk of malignancy
SUMP	Salivary gland neoplasm of uncertain malignant potential
SM	Suspicious for malignancy
USG	Ultrasound guided

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INTRODUCTION

Salivary glands form an important set of exocrine glands that function to produce, modify and secrete saliva into the oral cavity. These glands are divided into major salivary glands which includes parotid gland, submandibular gland and submental gland. Minor salivary glands are numerous in number and are found lining the mucosa of the mouth and upper aerodigestive tract. [1]

The cytology of normal salivary gland consists of acinar cells, ductal epithelial cells and scant fibrovascular stroma.

Acinar cells could be serous or mucinous in nature, appear as regular spherical acini delineated by their basement membrane, held together by small amount of fibrovascular stroma.

Ductal epithelial cells are found as small cohesive sheets or tubules having small cells with dense cytoplasm and round nucleus.

Fine needle aspiration cytology (FNAC) is being employed for preoperative diagnosis of salivary gland lesions for many years. It is a favoured method for diagnosis of salivary gland lesions due to their superficial nature and easy accessibility of the procedure. [2]

Salivary gland neoplasm comprise nearly 6.5% of all the lesions sampled in the head and neck, amongst these, nearly 40% are malignant. Use of ultrasound guidance (USG) and/or magnetic resonance imaging helps in imaging characteristics and the localization of the lesion within the salivary gland. Fine needle aspiration cytology is a highly reliable technique for preoperative diagnosis of salivary gland lesions. It has garnered widespread use and acceptance among clinicians and their patients. Majority of the salivary gland lesions are easily accessible for FNAC either superficially by palpation or by imaging techniques such as USG. Because of the minimally invasive nature of this technique, it is well tolerated by patients without any major complications. Also, it is a cost effective diagnostic tool with a high sensitivity and specificity. It provides prognostic information and sample for ancillary testing such as molecular genetic

studies. It provides useful information such as differentiating a neoplastic lesion from a non-neoplastic one and further recognizing the lesion as benign or malignant. [3]

Given the wide diversity of tumors arising in the salivary glands, there are many diagnostic challenges within the salivary gland cytopathology. Milan system for reporting salivary gland cytopathology is the recent standardized international reporting system for the classification of the salivary gland lesions which categorizes cytology into 6 categories namely: [4]

1. Non diagnostic
2. Non neoplastic
3. Atypia of undetermined significance
4. Neoplastic (Further categorized into Benign and Salivary gland neoplasm of uncertain malignant potential)
5. Suspicious for malignancy
6. Malignant

These categories are designed to reflect the everyday practice of salivary gland cytopathology, maximize communication between cytopathologists and clinicians, and provides estimates of reproducibility and malignancy risk.

AIMS AND OBJECTIVES

To study the detailed cytomorphological features of all salivary gland lesions and categorize them according to the Milan system for reporting salivary gland lesions.

REVIEW OF LITERATURE

Salivary glands are an important set of exocrine glands that function to produce, modify and secrete saliva into the oral cavity. These glands are divided into major salivary glands which includes parotid gland that extends from tip of mastoid to just below the angle of mandible, submandibular gland that lies between the anterior and posterior bellies of digastric muscle and submental gland which lies submucosally in the floor of mouth. And minor salivary glands lining the mucosa of the mouth and upper aerodigestive tract. [1] Salivary gland lesions form about 2-6.5% of all head and neck lesions. These lesions, especially those involving parotid and submandibular gland, are easily discernible owing to their superficial location. Fine needle aspiration cytology (FNAC) is being employed for preoperative diagnosis of salivary gland lesions for many years. It is a popular method for diagnosis of salivary gland lesions due to their superficial nature and easy accessibility of the lesion, hence minimal associated morbidity coupled with cost effectiveness. [2,3]

FNAC in salivary gland lesions is a useful method to evaluate suspicious lesions pre operatively and further categorize done into malignant or benign or intermediate and in some cases reach a specific diagnosis, hence playing a crucial role in disease management.

Salivary gland neoplasms comprise approximately 6.5% of the lesions sampled in the head and neck region amongst which 21%-46% are malignant. [3] Given the wide morphological diversity and overlapping features of tumors arising in salivary glands, there are many diagnostic challenges and pitfalls for salivary gland cytopathology. [5] Previous authors have generally attempted to render diagnosis similar to those given by surgical pathologist that reviewed histology, both biopsy or resection specimen. [6] Thus, very precise diagnosis were given in most of the series with attempts made to definitively classify adenomas into categories like pleomorphic, basal cell, myoepithelioma or Warthin tumor

while, when only benign salivary gland tissue was seen, the diagnosis generally rendered was “benign Salivary gland tissue with no pathological change”. These challenges were further amplified by the fact that several low-grade carcinomas significantly overlap with their benign counterparts. [7, 8]

This led a group of experienced cytopathologists and histopathologists to attempt to create a uniform cytological reporting scheme. This system is based on key principles developed for standardized terminology systems adopted for other body sites like uterine cervix, thyroid, pancreas.[9,10] The standardization effort started in September 2015 at the European Congress of cytology which was held in Milan, Italy under the umbrella of the American Society of Cytopathology (ASC) and the International academy of cytology. Subsequently an international panel of cytopathologists was organized to establish “The Milan System for Reporting Salivary Gland Cytopathology (MSRSGC).” [11]

The objective of the MSRSGC is to standardize terminology leading to better communication between clinicians and between institutions in order to improve overall patient care. This has brought consistency to the diagnosis and reporting on universal basis.

The establishment of classification system for reporting salivary gland FNA represents an essential step towards improving the overall effectiveness of salivary gland FNA, leading to improved patient care.

It emphasizes risk stratification rather than specific diagnoses, providing a Risk of malignancy for each ascending risk category rather than a binary benign or malignant assessment for each individual case

The Milan system categorizes salivary gland lesions into 6 categories, which are described as follows:

1. Non diagnostic [12]

This includes cases with:

-Insufficient quantitative and/or qualitative cellular material to make a cytological diagnosis.

-Aspirates with benign elements only, in a setting of clinically or radiologically defined mass

-Nonmucinous cyst contents.

The recommended criteria of cellularity is a minimum of 60 lesional cells

Exceptions to these cytologic criteria include the following:

a. Any salivary gland aspirate with significant cytologic atypia

b. Mucinous cyst fluid contents without an epithelial component.

c. The presence of abundant inflammatory cells without an epithelial component.

d. In the absence of neoplastic cells, the presence of a matrix component is suggestive of a neoplasm should not be classified as “Non-Diagnostic.”

2. Non Neoplastic [13]

The non-neoplastic lesions of the salivary glands are relatively common, and can clinically mimic a neoplasm due to the presence of a distinct mass.

This includes specimen lacking evidence of neoplastic process.

Inflammatory, metaplastic, infective and reactive lesions such as

a) Acute sialadenitis- In which abundant neutrophils ± bacteria, histiocytes necroinflammatory debris (suppurative) and granulation tissue in the later stages can be seen

b) Chronic sialadenitis- The combination of a hypocellular aspirate with absent acinar cells, small cohesive ductal groups, and mild chronic inflammation along with fibrotic stromal fragments

c) Granulomatous sialadenitis- Scant acinar and ductal cells along with groups of epithelioid histiocytes with variable amounts of acute and chronic inflammatory cells, it may have multinucleated giant cells and necrotic background debris

d) Sialadenosis- It predominantly affects the parotid gland and is usually present bilaterally. It is seen as a cellular aspirate composed of clusters of enlarged or hypertrophic acinar cells with maintained normal cytoarchitectural arrangement of acini in a background of stripped acinar

cell nuclei. Fibroadipose tissue is usually seen, however features suggestive of neoplasm, cyst, or inflammatory lesion are absent.

e) Sialolithiasis- Hypocellular smears with scant or absent acinar cells having groups of benign ductal cells and/or metaplastic squamous, ciliated, or mucinous cells in an inflammatory background. Calcifications (stone fragments) may be present

f) Lymphoepithelial sialadenitis (LESA) show cellular aspirates constituting of cohesive sheets of ductal cells, often with squamous metaplastic changes, and with small mature lymphocytes percolating through the epithelial sheets. Mixed population of lymphocytes, dendritic cells, and tingible body macrophages with predominance of small mature lymphocytes is usually present along with lymphohistiocytic aggregates. Acinar cells are usually absent.

A note is added as: Clinicoradiological correlation is essential to ensure that the specimen is representative of the lesion.

3. Atypia of Undetermined Significance (AUS) [14]

Salivary gland FNAC that lacks either qualitative or quantitative cytomorphological features to be diagnosed with confidence as non-neoplastic or neoplastic.

In addition, it also includes the FNAC exhibiting an atypical cytomorphologic feature that excludes the possibility of classifying it as “Non-Diagnostic.” Most samples will represent reactive atypia or poorly sampled neoplasms.

Salivary gland FNAs with suboptimal cellularity or with artifacts can raise uncertainty as to whether the aspirated lesion is neoplastic or not hence the cytological criteria for an aspirate to be labelled as AUS includes the following

a) Reactive and reparative atypia which is indefinite for a neoplasm

b) Squamous, oncocytic, or other metaplastic changes that are indefinite for a neoplasm

c) Low cellularity specimens that are suggestive of, but are not diagnostic of a neoplasm

d) Specimens with preparation artifacts that hamper distinction between a non- neoplastic and neoplastic process.

e) Mucinous cystic lesions with very scant or absent epithelial component.

f) Salivary gland lymphoid lesions or lymph nodes that are indefinite for a lymphoproliferative disorder

4. Neoplasm [15]

Salivary gland neoplasms are rare and more commonly occur in the parotid gland.

These comprise approximately 6% of all head and neck tumors, and 0.3% of all malignancies.

Fine-needle aspiration is widely utilized in the management of salivary gland neoplasms. It can effectively distinguish with high specificity (97–98%) a non-neoplastic lesion from a neoplasm and a benign neoplasm from a malignant neoplasm. FNA can diagnose the most common benign tumors of the salivary gland. However, FNA is generally less effective in providing a specific diagnosis for certain other epithelial neoplasms of the salivary gland hence the neoplastic category is further divided into 2 categories-

I. Benign neoplasm- Reserved for clear cut benign epithelial and mesenchymal neoplasms like Pleomorphic adenoma, Warthins tumor, Oncocytoma (epithelial in origin), Lipoma, Schwannoma, Lymphangioma, Hemangioma (mesenchymal in origin)

II. Salivary gland neoplasm of uncertain malignant potential (SUMP)- Reserved for FNAC specimens that are diagnostic of a neoplasm, however, a diagnosis of specific entity cannot be made. [16]

The differential diagnosis includes both benign and malignant tumors.

SUMP is further subcategorized into 3 categories –

(A) Cellular basaloid neoplasm

(B) Cellular oncocytic/oncocytoid neoplasm and

(C) Cellular neoplasm with clear cell features.

(A) Cellular basaloid neoplasm [17]

The morphologic scenarios and differential diagnosis of cases that are classified as SUMP “basaloid neoplasm” include

(i) Cellular basaloid neoplasm with fibrillary stroma - Cellular pleomorphic adenoma, Epithelial-myoepithelial carcinoma, Basal cell adenoma/adenocarcinoma

(ii) Cellular basaloid neoplasm with hyaline stroma - Basal cell adenoma/adenocarcinoma, Adenoid cystic carcinoma, Epithelial-myoepithelial carcinoma, Polymorphous adenocarcinoma

(iii) Cellular basaloid neoplasm with mixed/other stroma - Adenoid cystic carcinoma, Polymorphous adenocarcinoma

(iv) Cellular basaloid neoplasm with scant to no stroma - Cellular pleomorphic adenoma, Canalicular adenoma, Myoepithelioma, Myoepithelial carcinoma, Adenoid cystic carcinoma

B) Cellular oncocytic/oncocytoid neoplasm [18]

The morphologic scenarios and differential diagnosis of cases that are classified as SUMP “Cellular oncocytic/oncocytoid neoplasm” include

(i) Cellular oncocytic/oncocytoid neoplasm with Cystic background (histiocytes, proteinaceous debris, ± inflammatory cells- these include Warthin tumors, Cystadenoma oncocytic type

(ii) Cellular oncocytic/oncocytoid neoplasm with Mucinous background – these include mucoepidermoid carcinoma, oncocytic variant, rare case of Warthin tumor with focal mucinous/metaplastic change

(iii) Cellular oncocytic/oncocytoid neoplasm with Blood or non-specific background - includes Oncocytoma and Myoepithelioma

(iv) Cellular oncocytic/oncocytoid neoplasm with Granular (usually coarse)/vacuolated cytoplasm- includes Acinic cell carcinoma, Secretory carcinoma / Mammary analogue secretory carcinoma (MASC), Metastatic renal cell carcinoma

(v) Cellular oncocytic/oncocytoid neoplasm with appreciable focal nuclear atypia which includes Salivary duct carcinoma, High grade mucoepidermoid carcinoma, Metastatic carcinoma. However, it should be noted that cases with multifocal or diffuse presence of nuclear atypia should be classified as “suspicious for carcinoma” or “malignant”

C) Cellular neoplasm with clear cell features [19]

This includes a broad range of benign and malignant neoplasms with overlapping cytomorphologic features; the key diagnostic features include-

i. Lesional cells with clear or vacuolated cytoplasm.
ii. Neoplastic cells with clear cell features: Clear, foamy, granular, or vacuolated cytoplasm, or any combination with features that are not characteristic of true oncocytes

It is noted that up to 80% of salivary gland neoplasms arising in the parotid gland are benign, as compared to a significantly increased incidence of malignant tumors in the other major and all minor salivary glands.

5. Suspicious For Malignancy [20]

This category includes aspirates which are highly suggestive of malignancy but not definitive. It represents indeterminate diagnostic category in the Milan System which is used to stratify the risk of malignancy (ROM) and to inform the treating clinician that a particular specimen cannot be placed into a more specific benign or malignant diagnostic category due to diagnostic limitations such as sparse cellularity or various specimen artifacts. The purpose of separating SM from the Malignant category is to preserve the high positive predictive value (PPV) of a fine-needle aspiration classified as Malignant while at the same time offering a diagnostic option with a relatively high ROM for those aspiration where the cytomorphologic criteria fall short in quantity and/ or quality for a malignant diagnosis. These include cases with high grade carcinomas with limited sampling or other limitation.

The cytological criteria for an aspiration to be labelled as suspicious for malignancy includes

i. Markedly atypical cells with poor smear preparation, fixation artifact, poor cell preservation, or obscuring inflammation and blood
ii. Presence of limited cytologic features of a specific malignant lesion (e.g., adenoid cystic carcinoma, mucoepidermoid carcinoma, and acinic cell carcinoma) in an otherwise scantily cellular aspirate
iii. Presence of markedly atypical and/or suspicious cytologic features in a subset of cells admixed along with features of a benign salivary gland lesion. Atypical features include prominent nucleoli or macronucleoli, anisonucleosis, increased nuclear to cytoplasmic ratio, nuclear molding, prominent nuclear pleomorphism, atypical mitosis, and clumped or coarse chromatin.
iv. Scanty sample with atypical features suggestive of a neuroendocrine neoplasm

6. Malignant [21]

Aspirates which are diagnostic of malignancy. These can be subclassified into specific type and grades of carcinomas.

A majority of malignant tumors occur in the parotid and submandibular glands and accounting for most of the salivary gland fine-needle aspirations.

Salivary gland aspirates that are classified as “Malignant” usually contain a combination of cytomorphologic features that, either alone or in combination with ancillary studies, are diagnostic of malignancy. Whenever possible, an attempt is made to provide the grade of the neoplasm as well as the specific tumor type.

The entities included in it are –

(A) Low grade carcinomas

(a) **Acinic cell carcinoma** [22]

The criteria for an aspiration to be labeled as Acinic cell carcinoma include-

I. Cellular smears with predominantly dispersed or loosely cohesive cell population having “monotonous” population of epithelial cells.
II. The tumor cells are polygonal in shape with low nuclear–cytoplasmic (N:C) ratio with minimal nuclear pleomorphism and abundant delicate vacuolated basophilic cytoplasm.
III. Variable numbers of cytoplasmic zymogen granules are present which are PAS- positive, diastase resistant.
IV. Capillary meshwork with loosely adherent cells or well-developed papillary formation
V. No mitotic activity or necrosis is minimal.

Background is usually clean or frothy with few stripped nuclei.

(b) **Secretory carcinoma** [23]

The criteria for an aspiration to be labeled as secretory carcinoma includes –

I. Aspirates are cellular.
II. Cells can be present singly and in tubular, follicular, and papillary groups which appear bland cuboidal, polygonal with low N:C ratio having uniform round eccentrically located nuclei with smooth nuclear contours, fine chromatin and distinct nucleoli with abundant vacuolated eosinophilic cytoplasm.
III. Cytoplasmic zymogen granules are absent
IV. Uniform round eccentrically located nuclei with smooth nuclear contours, fine chromatin, and distinct nucleoli
V. Background constitutes of mucoproteinaceous material.

(c) **Epithelial-Myoepithelial Carcinoma** [24] - the criteria for an aspiration to be labeled as Epithelial-Myoepithelial Carcinoma includes-

I. Cellular aspirate with cells arranged in pseudopapillary groups, sheets, and 3 dimensional groups.
II. Predominant population of clear myoepithelial cells with minor population of ductal cells with scant cytoplasm.

III. Laminated, acellular stromal cores and stripped nuclei are present in the background.

IV. Biphasic nature of the tumor is highlighted by immunostaining with HMW keratins and myoepithelial markers such as P63, smooth muscle actin, calponin

(B) High-Grade Carcinomas

These include the following carcinomas –

(a) **Salivary Duct Carcinoma** [25] – criteria included are as follows

I. Cellular aspirate with sheets, three-dimensional crowded and cribriform groups of cells with overtly malignant cytologic features

II. Cells are medium to large polygonal with well-defined cell borders and abundant eosinophilic cytoplasm having enlarged round to oval, pleomorphic nuclei with anisonucleosis, hyperchromasia, and prominent nucleolus with frequent mitoses.

III. Background is necrotic with presence of stripped enlarged nuclei.

(b) **Lymphoepithelial Carcinoma** – Criteria -

Cellular aspirate with syncytial clumps of polyhedral to spindled cells with scant cytoplasm having pleomorphic, vesicular nuclei with distinct nucleoli with presence of abundant small background lymphocytes and plasma cells

(C) Cancers with Indeterminate or Multiple Grades

(a) **Mucoepidermoid Carcinoma** [26] – Criteria included –

I. Variable cellularity depending on the grade of the tumor.

II. Admixture of goblet-type mucus cells, intermediate, and epidermoid cell. Low-grade tumors containing more mucinous cells and high-grade tumors having a predominance of epidermoid cells.

III. Variable nuclear atypia from mild to markedly atypical.

IV. Variable presence of clear cells, oncocytic cells and columnar cells.

V. Cystic background with abundant extracellular mucin in low and intermediate grade tumors.

(b) **Adenoid Cystic Carcinoma** [27] - Criteria included -

I. Variably cellular aspirate with cohesive groups of basaloid cells arranged in small syncytial sheets with irregular borders, sometimes showing microcystic sieve like spaces, clusters, “cylinders,” and tubules.
II. Uniform, small basaloid tumor cells with high N:C ratio with scant, indistinct cytoplasm.
III. Bland, oval to angulated hyperchromatic nuclei with indistinct nucleoli.
IV. Mitoses and necrosis are usually absent in the absence of high-grade transformation.
V. Acellular homogenous and translucent matrix with sharp borders

(c) **Myoepithelial Carcinoma** [28] - Criteria included –

I. Cellular aspirate with neoplastic cells arranged singly, in small clusters, sheets, and crowded groups.
II. Metachromatic stromal material is variably present as small globules, bands, and spheres.
III. Variable nuclear atypia (pleomorphism, nucleoli, mitoses, hyperchromasia), depending upon grade.
IV. Several cell morphologies including plasmacytoid, spindled, clear, and epithelioid with moderate amounts of glycogen-rich cytoplasm.
V. Intranuclear pseudoinclusions present.

(d) **Carcinoma ex Pleomorphic Adenoma** [29] - Criteria-

I. Cellular aspirate with usual component of carcinoma being high-grade carcinoma, usually salivary duct carcinoma.
II. Focal component of classical pleomorphic adenoma is present.

Other malignancies such as lymphomas, sarcomas and metastasis are also included in this category.

(e) Aspirates of **secondary cancers involving the salivary gland** exhibit the following cytologic features:

I. Cellular aspirate with usually high-grade nuclear features.

II. The cytomorphologic characteristics depend upon the tumor type; most common metastases are: Squamous cell carcinoma, melanoma, or cancers from distant sites (lung, breast, kidney)

The categories are designed to reflect the everyday practice of salivary gland cytopathology, maximize communication between cytopathologists and clinicians, provide estimates of reproducibility and malignancy risk.

Liron Pantanowitz et al reviewed the cytopathology of salivary gland cysts and classified cystic salivary gland lesions according to MSRSGC. [30] They divided salivary gland cysts based upon the presence of mucin and admixed lymphocytes in cyst fluid into mucinous and non-mucinous cysts which they further subcategorized into non neoplastic cysts and neoplastic cysts. The further distribution as highlighted in their study is as follows

(i) Non-diagnostic category - Cystic non-mucinous fluid only.

(ii) Non-neoplastic - Inflammatory cyst with amylase crystalloids

(iii) Atypia of undetermined significance – Histiocytes with scant or absent epithelial cells in a background of abundant mucin (which cannot exclude low grade mucoepidermoid carcinoma, Benign neoplasm like Warthin tumor, or cystic pleomorphic adenoma.)

(iv) Salivary gland neoplasm of uncertain malignant potential (SUMP)- Cellular oncocytic/oncocytoid neoplasm with cystic background (differential includes Warthin tumor or oncocytic cystadenoma)

(v) Suspicious for malignancy- Atypical cells in a mucinous background, suspicious for low-grade mucoepidermoid carcinoma

(vi) Malignant- Keratinizing squamous cell carcinoma

They concluded that a reliable approach to interpreting FNA specimens from patients with cystic salivary gland lesions is essential to accurately determine which of these patients may require subsequent surgery.

Ritu Jain et al, in their study included 80 patients who underwent pre-operative FNAC followed by surgical procedure and histologic examination. The histologic diagnosis was considered as the gold standard. Diagnosis of FNACs were compared with the final histologic

impression and concordance assessed. Sensitivity, specificity and diagnostic accuracy of FNAC for malignant lesions were also calculated. Of the 80 cases, majority (67.5%) involved the parotid gland. Eight cases (10%) were non-neoplastic lesions, and comprised of sialadenitis, retention cyst and sialadenosis. Of the remaining total 72 neoplasms, 58 were benign and 14 were malignant salivary gland tumors. A cyto-histologic concordance of benign diagnosis was achieved in 85.7% of cases and for malignancy in 92.8% of the tumors. FNAC had a sensitivity of 92.8%, specificity of 93.9%, a positive predictive value of 81.2% and negative predictive value of 98.4% for malignant salivary gland tumors. There was one false-negative and four false-positive diagnosis on FNAC. [31]

S.A. Thiryayi et al studied 287 salivary gland aspiration cytology samples received in their department for two years retrospectively and assigned a diagnostic category code from the MSRSGC. Cytology results were correlated with subsequent histology (where ever available), clinical and radiological follow up. The specimens were classified as 21.3% non-diagnostic, 22% non-neoplastic, 2.4% atypia of uncertain significance, 36.9% benign neoplasm, 5.2% neoplasm of uncertain malignant potential, 1.7% suspicious for malignancy and 10.5% malignant (low grade 1.4% and high grade 9.1%). Clinical/radiological follow up was available only for 145 patients (50.5%) and no follow up for the remaining 4 (1.4%) cases. The risk of malignancy for different categories was found to be 8.5% for non-diagnostic, 1.6% for non-neoplastic, 0% for atypia of uncertain significance, 1.9% for neoplasm benign, 26.7% for neoplasm of uncertain malignant potential, 100% each for suspicious for malignancy and malignant category. [32]

In another retrospective study conducted by Manish Rohilla et al over a period of 3 years (2014-2016) 631 cases were evaluated. The age of patients ranged from 1 to 95 years with the mean age being 43.7 years, M:F ratio was 1.7:1. The parotid gland was the most commonly involved

(61.3%) followed by submandibular gland (35.7%) and minor salivary glands (3%). No case of sublingual salivary gland lesion was observed in the study. There were no post FNAC complications in any of these cases. [19] Non diagnostic aspirations were found to be 2.2% (14 of the 631 cases). Non neoplastic lesions accounted for 55.8% (352 out of 631) whereas 40.4% (225 of 361) were neoplastic. Of the 225 neoplastic lesions 73.7% (188 of 225) were benign and 23.9% (61 of 225) were malignant. 1.6% cases were classified as cystic lesions and 2.4% cases were classified as neoplasms without further categorizations. [33]

A study conducted by Viswanathan K et al from 2011 through 2016 on total of 627 salivary gland FNA specimens, follow-up was available for 373 cases. The original diagnoses were recategorized using MSRSGC by 2 independent cytopathologists and the Risk of Malignancy (ROM) and overall ROM for each diagnostic category were determined, with characterization of "indeterminate" (AUS, SUMP, and SFM) lesions.[11] There was near-perfect agreement regarding categorization (626 of 627 cases; 99.8%) between the 2 cytopathologists, with discordance observed for 1 case. The sensitivity, specificity, negative predictive value, and positive predictive value of salivary gland aspirates at the study institution were 79%, 98%, 94%, and 92%, respectively. The risk of malignancy for non-diagnostic, non-neoplastic, benign neoplasms, AUS, SUMP, SFM, and malignant were 6.7%, 7.1%, 38.9%, 5.0%, 34.2%, 92.9%, and 92.3%, respectively. The indeterminate category had an overall ROM of 47.1%. [11]

A retrospective study conducted by Layfield LJ on One-hundred and sixty-four cases from a prior cytological study with histological follow-up were re-reviewed by one of the authors and that assigned to one of the MSRSGC categories. The original and MSRSCG diagnoses were compared, as were follow-up recommendations.

The MSRSGC system classified 29 specimens as non-diagnostic (of which, seven histologically were shown to be benign salivary gland, two

non-mucinous cysts, 14 sialadenitis, one pleomorphic adenoma, one haemangioma, one lymphoma, one adenoid cystic carcinoma, one squamous carcinoma and one benign lymphoid proliferation). In the original study these lesions were diagnosed as: seven benign cysts, fifteen benign salivary gland tissue, one benign neoplasm and two insufficient for diagnosis. In seven cases, MSRSGC disagreed with original diagnoses and surgical resection showed lesions where optimal follow-up was more consistent with original cytological diagnosis. In 10 cases with disagreement, the MSRSGC was associated with a more appropriate follow-up based on the surgical diagnosis. Malignancy risks for the Milan categories were: non-diagnostic (12%), non-neoplastic (5%), atypia of undetermined significance (19%), neoplasm, benign (5%), neoplasm (40%), suspicious for malignancy (60%) and malignant (93%). MSRSGC was comparable with the original reported diagnoses in the majority of cases. Both systems had high accuracy for distinguishing benign from malignant lesions and both were associated with appropriate follow-up in most cases. [4]

Erkka Tommola et al conducted a study over one-year-period (January 2018–December 2018) consisting of 183 salivary FNA samples from 138 patients with correlation to histopathology in 90 cases with surgical follow-up. The MSRSGC performance in patient based analysis was as follows: accuracy was 90.9%, sensitivity was 61.5%, specificity was 100%, positive predictive value was 100%, and negative predictive value was 89.4%, respectively. Risks of malignancy (ROMs) in MSRSGC categories were: 0.0% in non-diagnostic category, 100.0% in non-neoplastic category, 14.3% in atypia of undetermined significance category, 0.0% in benign neoplasm category, 27.3% in neoplasm of uncertain malignant potential category, and 100% for both suspicious for malignancy and malignancy categories respectively. Thus MSRSGC proved as a reliable classification system in salivary gland FNA routine diagnostics in their settings. [34]

Chayanika et al evaluated salivary gland FNAC of 293 cases according to age, sex, and site of involvement. Males were slightly more affected than female, the ratio being 1.1:1. Largest number of cases were seen in age group 21 to 40 year (46.1%) followed by 41–60 year age group (27%). Parotid gland was involved in 57.7% cases followed by submandibular gland in 27.3% with minor salivary gland involved in 15% of cases. Non neoplastic category was the largest category 38.2% followed by neoplastic benign category (33.4%). Malignant, Suspicious of Malignancy, Non Diagnostic, Atypia of Undetermined Significance, and Salivary gland neoplasm of Uncertain Malignant Potential (SUMP) constituted 15%, 2.4%, 6.1%, 2.7%, and 2%, respectively. Histological follow-up was available in 172 cases. In category 1 (Non-Diagnostic); out of 18, follow-up was available in only 4 cases, and out of these, 1 case turned out to be adenoid cystic carcinoma on histological follow-up. The overall ROM for this category reported was 25%. In category 2 (Non-Neoplastic), histological follow-up of 20 cases were available; out of total 112 cases, 3 cases of benign tumor were reported, which were wrongly diagnosed as chronic sialadenitis, and 1 case of mucoepidermoid carcinoma (MEC) was reported on histopathology, which was interpreted as -granulomatous sialadenitis on FNAC into category 2. The overall ROM reported for this category was 5%. In category 3 (Atypia of undetermined significance) -histological follow-up was available for 5 out of 8 cases. Three cases were reclassified as pleomorphic adenoma (PA), 1 case as basal cell adenoma (BCA), and 1 case was reclassified as adenoid cystic carcinoma (AdCC). Overall, ROM for this category was 20%. Category 4a had histological follow-up of 90 cases out of 98 cases. Out of 75 cases diagnosed as PA on FNAC, 71 cases were concordant on histological follow-up, and 4 cases reclassified into malignant category. The overall ROM reported was 4.4% in this category. In category 4b those cases were included where a specific neoplastic entity cannot be made, and out of 6 cases, 1 case was reclassified as granulomatous sialadenitis, 3 cases as

PA, and 1 case as AdCC and MEC each. Overall, ROM reported was 33.3% in this category.

Category 5 had histological follow-up of 7 cases, and 6 cases were concordant with diagnosis of malignancy with ROM of 85.7%. Category 6 included those smears that are diagnostic for malignant lesion, and histological follow-up of 40 cases was available. Only one case was misdiagnosed as malignant on FNAC, which was reported as PA on histological follow-up. Twelve cases of MEC, 13 cases of AdCC, 4 cases of lymphoma, 3 cases of carcinoma ex pleomorphic adenoma, 2 cases of epithelial myoepithelial carcinoma, acinic cell carcinoma, and polymorphous adenocarcinoma each, and 1 case of lymphoepithelial carcinoma were reported, and overall risk of malignancy reported was 97.5% for this category. [35]

Deepika Savant et al conducted a 6-year retrospective study from 2011 to 2016, constituting 331 cases of salivary gland lesions with cytologic interpretation. Of these 199 cases that had surgical resection specimens were included in the study. Metastatic tumors were excluded.

The distribution of cases according to the MSRSGC diagnostic categories was: nondiagnostic 9%, non-neoplastic 2%, atypia of undetermined significance (AUS) 6%, benign neoplasm 59.5%, salivary gland neoplasm of uncertain malignant potential 11%, suspicious for malignancy 1.5% and malignant 11%.

Based on the diagnosis of the corresponding resection specimen, the ROM for each of the diagnostic categories was determined as 0% for non-diagnostic and non-neoplastic, 33% for AUS, 0.84% for benign neoplasms, 40.9% for SUMP and 100% for both suspicious for malignancy and malignant cases. The cytologic diagnosis of the reviewer was found to be concordant with the original diagnosis in all but one case. The ROM reported in their study was mostly concordant with ROM published by the MSRSGC implying that the classification is helpful in planning management for various categories of MSRSGC. [36]

MATERIALS AND METHODS

Source of Data

Fine needle aspiration smears from salivary gland lesions were received in the Department of Pathology of Dayanand Medical College and Hospital, Ludhiana over a period of five years [(1st July 2015 – 30th June 2020) three and a half years retrospective and one and half years prospective].

METHOD OF COLLECTION OF DATA

A study of patients undergoing fine needle aspiration (FNA) of salivary gland lesions over a period five years [three and a half years retrospective and one and half years prospective (1st July 2015 – 30th June 2020)] was done in this study. After informed consent, percutaneous or imaging guided fine needle aspiration (FNA) was done using 21 gauge needle attached to 20cc disposable plastic syringe in patients. PT-INR was taken into account for image guided aspiration where values didn't exceed 1.5. Taking aseptic precautions, needle was introduced into the lesions / swellings, 6-8 slides were prepared immediately. One of the slide was utilized for rapid on site evaluation for adequacy by doing the Toulidine blue stain. Two of them were wet fixed in 95% ethanol and stained with Papanicolaou stain, Hematoxylin and Eosin and the remaining smears were air dried and stained by May Grunwald Giemsa stain. FNA sample was collected in a separate pass and fixed in 10% formalin, processed and embedded to make a cell block. Sections were stained by H & E stain. Special stains were done wherever necessary. Cytopathological-histopathological correlation was done wherever possible.

INCLUSION CRITERIA

FNAC samples from salivary gland lesions received in the cytology laboratory of the pathology department which included

1. FNAC samples performed in the department through direct procedure.

2. FNAC slides received in the department after guided aspiration under image (ultrasonography and CT) guidance.
3. Prepared and stained slides for review from an outside centre.

EXCLUSION CRITERIA

Samples obtained from lesions other than from salivary gland origin.

OUTCOME

The smears obtained by FNA of all salivary gland lesions were analysed in this study and categorized according to the Milan system of reporting salivary gland lesions. The cytological findings were correlated with the clinico-radiological profile, cell block findings, histopathological findings, special stains and IHC findings wherever possible.

MATERIAL USED

1. Cameco's syringe pistol
2. Disposable 20 ml syringe
3. Needle 21G/ 23G
4. Glass slides
5. Spirit swab
6. Dry swab / cotton gauge
7. Disposable gloves
8. Diamond pencil for marking slides
9. FNAC reporting form
10. Tray for carrying slides

PROCEDURE DONE

After informed consent, percutaneous fine needle aspiration (FNAC) was done using 21 guage needle for salivary gland lesions attached to 20cc disposable plastic syringe. Taking aseptic precautions, needle was introduced in lesion/swelling, slides were prepared immediately. One of the slide was utilized for rapid on site evaluation for adequacy by the Toulidine Blue stain. Two of them were wet fixed in 95% ethanol and stained with Papanicolaou stain and Hematoxylin and Eosin stain .The remaining smears were air dried and stained by May Grunwald Giemsa

stain. FNA sample collected in a separate pass was fixed in 10% formalin, processed and embedded to make cell blocks.

Staining of smear

1. Dry fixed smears were prepared by air drying and then fixing in methanol followed by staining with Giemsa

2. Wet-fixed smears were prepared by immediately fixing in 95% isopropyl alcohol and stained by H & E and Papanicolaou stain.

Giemsa Stain:

Giemsa stock

Geimsa stain powder 4 gm

Glycerol 250ml

Methanol 250ml

Giemsa working solution

Giemsa 4ml

Distilled water 96ml

Procedure:

1. Smears were air dried and fixed with methanol.

2. Giemsa stain 1 in 10 dilutions (9ml water, 1ml Geimsa stain) was poured over the slides to cover whole of the smear for 10 minutes.

3. Stain was removed and slides washed with distilled water thoroughly and air dried.

4. Mounting in DPX.

Hematoxylin & eosin

Stain solutions:

Harris's Hematoxylin

Hematoxylin 2.5 gm

Absolute alcohol 25ml

Potassium alum 50 gm

Distilled water 500 ml

Mercuric oxide 1.25 gm or

Sodium iodate 0.5gm

Glacial acetic acid 20ml

Eosin 1% (commercially available)

95% Ethyl alcohol

Acid alcohol

1% Ammonia

Acetone

Xylene

1) The smears were fixed with 95% rectified spirit or ethyl alcohol and kept for ½ hour.

2) Then ten dips each were given in 80%, 70%, 50% alcohol.

3) Washed in distilled water-10 dips.

4) Harris hematoxylin- 3 mins.

5) Washed in running tap water till excess stain was removed - 1 min.

6) Acid alcohol 0.5% HCl -10 dips.

7) Washed in running tap water- 30 secs.

8) 1% ammonia -3 dips

9) 95% alcohol -10 dips.

10) Eosin - 20 dips

11) Acetone -10 dips

12) Acetone - 10 dips

13) Xylene -10 dips

14) Xylene -10 dips

Papanicolau Stain requirements

Stain Solutions:

Harris Haematoxylin

Hematoxylin 2.5gm Distilled water 500ml

Mercuric oxide 1.25 gm or Absolute alcohol 25 ml

Sodium iodate 0.5 gm Potassium alum 50 gm

Glacial acetic acid 20 ml

Orange G 6

10% aqueous Orange G 50 ML

Alcohol 950 ml

Phosphotungstic acid 15 gm

Eosin alcohol 36

0.5% light green 0.5% Eosin

0.5% Bismarck brown 95% ethyl alcohol

Phosphotungistic acid Glacial acetic acid

Lithium carbonate Absolute methanol

Procedure

1) The smears are wet fixed with 95% rectified spirit for half an hour.
2) Then ten dips each were given in 80%, 70%, 50% alcohol.
3) Washed in distilled water.
4) Stained with harris‟s haematoxylin 0-3 mins.
5) Washed in running tap water.
6) Given 10 dips in 1% ammonia.
7) Washed in running tap water.
8) Dipped in 95% alcohol-10 dips.
9) Kept in orange- G 6 for 30 secs.
10) Given 10 dips in 95% and repeated again.
11) Kept Eosin Alcohol 36 for 2 mins.
12) Acetone – 10 dips.
13) Again acetone 10 dips.
14) Xylene – 10 dips.
15) Again xylene – 10 dips.
16) Mounted slide with DPX.

Ziehl –Neelsen (ZN) stain Requirements

Carbol fuschin

Basic fuschin- 0.5 gm

Absolute alcohol-5 ml

5% aqueous phenol-100 ml

Mix well & filter before use.

Methylene blue solution (stock)

Methylene blue-1.4 gm

95% Alcohol -100 ml

Working methylene blue solution (working)

Methylene blue -10 ml

Tap water-90 ml

20% sulfuric acid

(1% sulphuric acid for Nocardia, 5% sulphuric acid for Mycobacterium tuberculosis)

Procedure

1. Make a smear and allow it to dry at room temperature.
2. Flood the slide with carbol fuschin and heat gently until the steam is seen rising from the slide. Do not bring to boil.
3. Heat intermittently for 10 mins.
4. Wash well in tap water.
5. Differentiate in acid alcohol (2-5 dips).
6. Flood the slide with 20% sulphuric acid. Leave this until the smear is pale pink in color.
7. Rinse in tap water.
8. Counterstain with methylene blue till smear is pale blue.
9. Rinse in tap water.

PAS Stain (Periodic Acid Schiff Stain)

Components:

1% periodic acid

Schiff reagent

- Distilled water 100ml
- Basic fuschin 1gm
- Sodium metasulphite 2gm
- 1N HCL 20ml
- Activated charcoal 0.3mgm

Sodium metasulphite solution

Stock solution 10% aqueous solution

Working solution 5% of stock solution + 100 ml distilled water

Oxalic acid 0.5 gm

Potassium sulphite 0.5 gm

Distilled water 100 ml

1% acetic acid 100ml

Fixation – 70% ethyl alcohol

50% ethyl alcohol

1% hematoxylin

Procedure

1. Give 15 dips in distilled water
2. Pour Periodic acid for 10 minutes
3. Wash under running tap water for 10 minutes
4. Pour distilled water for 15 minutes
5. Pour Schiff reagent for 15 minutes
6. Pour Sodium metasulphite 6 minutes
7. Wash under running tap water for 10 minutes
8. Pour Hematoxylin for 4 minutes
9. Wash under running tap water for 5 to 10 minutes
10. Wash under running tap water for 5 minutes
11. Pour distilled water and keep for 5 minutes
12. Give 15 dips in distilled water
13. Give 15 dips in 95% ethyl alcohol
14. Give 15 dips in 95% ethyl alcohol
15. Give 15 dips in absolute alcohol
16. Give 15 dips in absolute alcohol
17. Give 15 dips in xylene

Procedure to make cell block

1. A separate pass was given to collect material for making cell blocks.
2. Suck 20 ml of 10% formalin into the syringe immediately.
3. Put the material with formalin into test tube and leave for 6 hours.

4. Centrifuge the material for 5 minutes and wash with phosphate buffered saline (PBS).Repeat it 3 times.

5. Put 100 ml pooled plasma into button and mix it.

6. Add 25-40 ml of thrombin segment.

7. Leave till the clot is formed.

8. Give it for tissue processing.

Immunohistochemistry - **standard Strept Avidin Procedure**

1. 2-3 mm sections were cut and mounted on Poly L-lysine coated slides. Slides were dried overnight at 37°C and dewaxed in xylene and hydrated.

2. Sections were put on Poly L-lysine coated slides and incubated at 60°C for 30 min. The temperature was adjusted at 37°C after 30 minutes. The slides were left in incubator for overnight.

3. All slides were dewaxed by heating with spirit lamp. Xylene 3 changes for 10 minutes xylene/ alcohol 1 change for 10 minutes 100% alcohol 1 change for 5 minutes 95% alcohol 1 change for 5 minutes 80% alcohol 1 change for 5 minutes 70% alcohol 1 change for 5 minutes Finally all slides were rinsed in running tap water.

4. Antigen retrieval procedure - The black box was filled 3/4th with citrate buffer and the slide carrier with slides was placed in it.

5. The black box was placed in microwave for 9 min.

6. Boiling of the solution was observed and the microwave was reset for 6 min and started.

7. The box was removed and cooled in running tap water.

8. Blocking endogenous peroxidase-sections were incubated at room temperature in 0.3% H_2O_2 in methanol for 30 to 45 minutes and rinsed in running tap water for 5 to 10 minutes, and dipped in distilled water for 1 minute.

9. The slides were placed in Tris buffer (only 1 change for 5 min).

10. Blocking reagent was applied for 5 - 10 min. The excess blocking reagent was wiped off.

11. Primary antibodies were applied covering the whole tissue and incubated at room temperature for 1 hours.

12. Slides were then washed in Tris buffer for 5 minutes (4 changes).

13. The slides were cleaned with tissue paper. 56

14. Ultra Vision One HRP Polymer covering the whole tissue was applied and incubated at room temperature for 45 minutes.

15. Washing was done in TBS buffer (Tris buffered saline) for 5 minutes (4 changes).

16. One drop of substrate- DAB (3,3-Diaminobenzidine) solution was applied on each slide covering the whole material.

17. lncubated for 10-1 5 min.

18. All slides were washed in deiodinized water.

19. Hematoxylin was applied for few seconds.

20. The slides were put in running tap water.

21. They were allowed to dry and dehydrate in alcohol.

22. Incubated for 2 min and allowed to dry.

23. Mounted in DPX (distyrene dibutyl phthalate xylene).

24. The slides were examined microscopically.

STATISTICAL ANALYSIS: Data were described in terms of range; mean ±standard deviation (± SD), median, frequencies (number of cases) and relative frequencies (percentages) as appropriate. All statistical calculations were done using SPSS (Statistical Package for the Social Science) SPSS 21 version statistical program for Microsoft Windows.

OBSERVATIONS AND RESULTS

The present study was conducted on 160 cases of salivary gland lesions in the Department of Pathology over a period of 5 years from 1st July 2015 to 30th June 2020 (3.5 years retrospectively and 1.5 years prospectively). The FNAC smears were analyzed for cytomorphology and categorized according to the Milan system of reporting salivary gland cytopathology. The demographic findings, clinical data along with cytomorphological findings and histopathology diagnosis wherever available were recorded according to the proforma and the following observations were made.

Cytological categorization of salivary gland lesions according to Milan system of reporting salivary gland cytopathology. (MSRSGC)

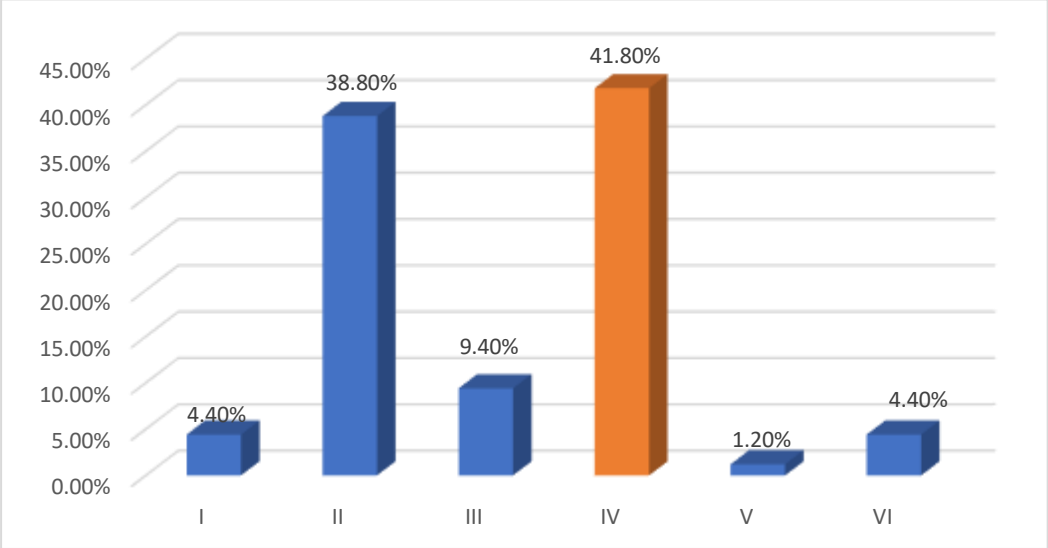
The establishment of MSRSGC for reporting salivary gland FNA represents an essential step towards standardizing terminology and hence improving the overall effectiveness of salivary gland FNA and improved patient care. The MSRSGC is a six tier international classification scheme with risk stratification comprising of Category 1- Non diagnostic, Category II – Non neoplastic, Category III- Atypia of undetermined significance (AUS), Category IV- Neoplastic which is subcategorized as Benign (IV a) and SUMP (IV b), Category V- Suspicious for malignancy and Category VI- Malignant

The cytological categorization of 160 cases according to MSRSGC was done.

Table 1: Distribution of cases according to MSRSGC (n-160).

Category	Classification			No of cases	Percentage
I	Non-Diagnostic			7	4.4%
II	Non-Neoplastic			62	38.8%
III	Atypia of Undetermined significance (AUS)			15	9.4%
IV	Neoplastic	IV a	Benign	57	35.6%
		IV b	SUMP	10	6.3%
V	Suspicious for malignancy (SM)			2	1.2%
VI	Malignant			7	4.4%

Fig. 1: Distribution of cases according to MSRSGC (n-160).



Category IV (Neoplastic) was the most common category comprising of 41.8% of the cases of which most of the cases were subcategorized as Benign. This was followed by category II (Nonneoplastic) comprising of 38.8% of the cases. The indeterminate categories i.e. categories III (AUS) and V (Suspicious for malignancy) had 9.4% and 1.2% of the cases respectively, while category I (Nondiagnostic) and category VI (Malignant) included 4.4% of the cases each. (Table 1, Fig. 1)

Age and sex prevalence

The age of the patients ranged from 6 years to 88 years with the highest number of patients in the age group of 41-60 years (42.8%). 53.7% of the cases were males while 46.3% of the cases were females with M:F ratio of 1.1:1

Table 2: Mean age and gender ratio of patients classified in various categories of MSRSGC (n-160).

MSRSGC Categories	Mean Age (years)	M:F Ratio
I (n-7)	51.29	0.75:1
II (n-62)	48.48	1:2
III (n-15)	49.20	2:1
IV benign (n-57)	48.84	1.1:1
IV SUMP (n-10)	52.50	0.4:1
V (n-2)	53.60	0.6:1
VI (n-7)		

Non neoplastic pathology was common in 5th decade of life with mean age of 48.48 years in comparison to the malignant lesions seen more commonly in 6th decade with a mean age of 53.6 years (Table 2)

Clinical presentation of the cases

The lesions were analysed according to the clinical presentation including symptom, signs, co-morbidities and imaging studies.

(I)- Site (n-160)

The lesions under various categories of MSRSGC were further subdivided depending on site of involvement as Major (parotid gland, submandibular

gland and submental gland) and Minor (oral mucosa and upper aerodigestive tract) salivary glands as follows

Table 3: Sites of involvement of various lesions in MSRSGC categories (n-160).

MSRSGC Category	Major salivary gland (n-154)					Minor Salivary gland (n-6)	
	Parotid (n-109)	Sub-mandibular (n-44)	Sub-mental (n-1)	**Total**	%	**Total**	%
I (n-7)	4	3	0	**7**	4.6%	**0**	-
II (n-62)	31	31	0	**62**	40.2%	**0**	-
III (n-15)	11	4	0	**15**	9.8%	**0**	-
IV a (n-57)	51	2	0	**53**	34.4%	**4**	66.6%
IV b (n-10)	8	1	0	**9**	5.8%	**1**	16.7%
V (n-2)	1	1	0	**2**	1.3%	**0**	-
VI (n-7)	3	1	1	**6**	3.9%	**1**	16.7%

Major salivary glands were more frequently involved. Minor salivary glands were found to be involved only in the neoplastic lesions (category IV, V and VI), while major salivary glands were involved by lesions belonging to all the categories. Parotid gland was the most common salivary gland involved followed by submandibular gland. (Table 3)

(II) Clinical Characteristic (n-160)

The size of the lesion, laterality, features of swelling such as circumscription, mobility, tenderness was taken into account along with size variation with meals.

Table 4: Clinical characteristics under categories of MSRSGC (n-160).

Characteristics		Classification under MSRSGC							Total	%
		I	II	III	IV a	IV b	V	VI		
Size (cm)	<2	7	44	13	31	7	1	5	**108**	67.5%
	2-5	0	18	2	24	3	0	2	**49**	30.6%
	>5	0	0	0	2	0	1	0	**3**	1.9%
Laterality	Unilateral	7	59	15	54	10	2	7	**154**	96.2%
	Bilateral	0	3	0	3	0	0	0	**6**	3.8%
Swelling Circumscription	Well Circumscribed	7	30	13	57	9	2	7	**155**	96.9%
	Diffuse	0	2	2	0	1	0	0	**5**	3.1%
Mobility	Mobile	1	2	3	0	0	0	0	**6**	3.8%
	Immobile	6	60	12	57	10	2	7	**154**	96.2%
Pain	Present	0	8	0	1	0	0	2	**11**	6.8%
Size variation with meals	Exaggerated after eating	0	6	0	0	0	0	0	**6**	3.1%
Tenderness		0	3	0	0	1	0	0	**4**	2.5%

The size of lesions varied from 0.5 cm to 7cm, with majority of lesions (67.5%) measuring less than 2 cm while just 1.9% of lesions were found to

have size more than 5 cms. The lesions were predominantly unilateral, comprising of 96.2% of the total cases. The most common presenting symptom was swelling which was present in all the cases, of which, well circumscribed swelling was found in 96.9% of the cases, and mobile swelling in 3.8% of the cases. Painful swellings were seen in 6.8% of the cases majority of which were classified under inflammatory category. (Table 4)

(III) Co-Morbidities

Table 5: Co-morbidities in different categories of MSRSGC (n-160).

Co-Morbidities	Classification under MSRSGC							**Total**	%
	I	II	III	IV a	IV b	V	VI		
DM2	0	4	0	2	0	0	0	**6**	3.75%
K/C/O Ca	0	1	0	3	0	0	3	**7**	4.37%
Smoking/Tobacco chewing	0	5	2	4	1	2	0	**14**	8.75%

Antecedent history of Diabetes mellitus was present in 3.75% (6/160) of the cases, 4 of which were diagnosed in category II as Chronic Sialadenitis.

History of previous malignancy (Post op and post chemotherapy/radiotherapy that included 2 cases of breast carcinoma, 1 case of lung carcinoma, 3 cases of primary malignancy of salivary gland (1 case of mucoepidermoid carcinoma and 2 cases of adenoid cystic carcinoma respectively), and 1 case of carcinoma maxilla was found in (7/160) 4.37% of the cases. History of smoking/tobacco chewing was present in (14/160) 8.75% of the cases. (Table 5)

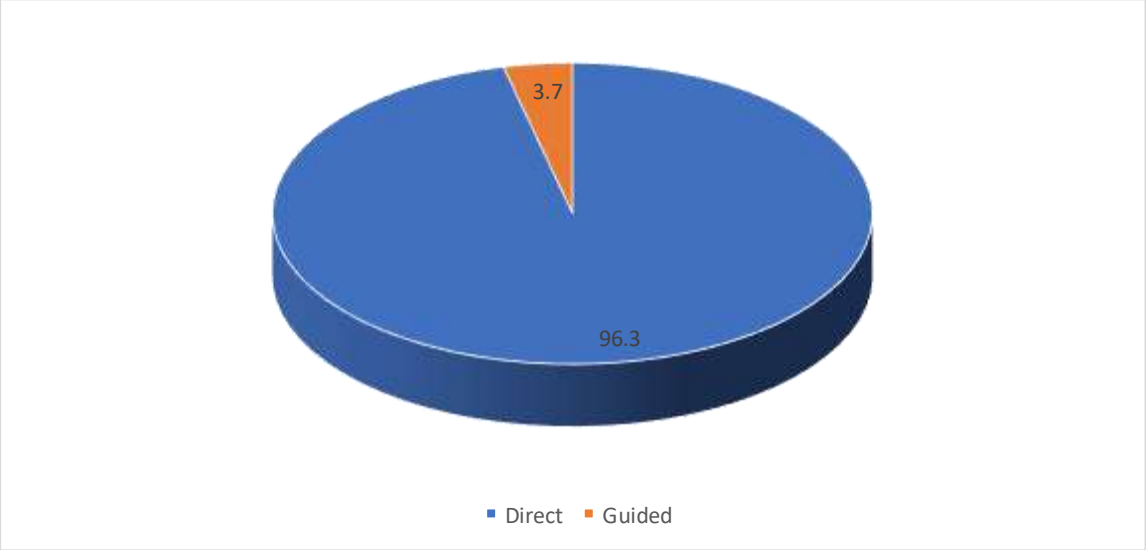
(IV) Radiological investigations

Radiological investigations (ultrasonography, CT or MRI) were available in 51/160 (31.8%) of cases which revealed solid, cystic as well as complex lesions. Of these 90.1% lesion were solid while 5.8% were cystic and 3.9% had a complex lesion with both solid and cystic areas.

Table 6: Distribution of imaging findings according to MSRSGC categories (n-51).

Radiology	Classification under MSRSGC								
	I (n-2)	II (n-18)	III (n-6)	IV a (n-17)	IV b (n-3)	V (n-1)	VI (n-4)	**Total (n-51)**	%
Solid	2	17	3	16	3	1	4	**46**	90.2%
Cystic	0	1	2	0	0	0	0	**3**	5.9%
Complex	0	0	1	1	0	0	0	**2**	3.9%

Fig. 2: Distribution of cases according to mode of procedure (n-160).



Most common mode of procedure was found to be FNAC performed under direct vision. (96.2%). Six cases accounting for 3.7% of the cases underwent imaging guided procedure. A definitive diagnosis could not be

reached in 6 out of 154 cases in the FNAC performed under direct vision and 1 out of 6 cases in imaging guided FNAC (Fig. 2)

MSRSGC Category I - Non-Diagnostic [n-07, (4.4%)]

The adequacy criteria for a cytology smear from salivary gland to be considered as adequate, is presence of at least 60 lesional cells.

Smears were rendered non diagnostic if cellularity was less or preservation was compromised or when non neoplastic salivary gland elements were seen in the presence of a clinically or radiologically defined mass.

However, any salivary gland aspirate with significant cytologic atypia or presence of mucinous cyst fluid contents or abundant inflammatory cells without an epithelial component or matrix component suggestive of a neoplasm was considered satisfactory for evaluation.

A total of 7 cases were categorized under the Non-diagnostic category with mean age of patients being 51.2 yrs. The youngest patient was found to be 16 years old and eldest being 75 years old. The M:F ratio was found to be 0.75:1. All the swellings were well circumscribed and present unilaterally in the major salivary glands with parotid gland being the most common site. The size of lesion was less than 2 cm in diameter in all the cases. No association with pain, exaggeration of swelling while eating and signs of inflammation were seen. None of the patients had history of smoking or tobacco chewing. Two of the patients had a radiological investigation done which revealed a solid lesion. Ultrasound guided FNAC was performed in only one of the patients, while the remaining cases were sampled percutaneously under direct vision.

Table 7: Distribution of cases in MSRSGC category I according to Cause (n-7).

Cause	No of cases	Percentage
Insufficient cellularity	6	85.7%
Blood only	1	14.3%

85.7% of cases had scanty cellularity while 14.3% of the cases had only blood in the smears with insufficient epithelial cell elements/ matrix components/inflammatory cells/cyst fluid hence making the slides non diagnostic for evaluation.

No biopsy specimens were received and the cells blocks made were inadequate for opinion. Hence cyto-histopathological correlation or risk of malignancy could not be deduced for this category.

MSRSGC Category II - Non neoplastic [n – 62 (38.8%)]

This category included specimens lacking evidence of a neoplastic process. It included inflammatory (acute, chronic and granulomatous), metaplastic and reactive changes.

Sixty-two cases were put under this category. The mean age was 48.48 years with the youngest patient being 6 years old and eldest being 86 years old. The M:F ratio was found to be 1:2.

All the lesions involved major salivary glands with parotid gland and submandibular gland being equally affected.

Majority (95.1%) of the cases had a unilateral swelling with good circumscription in 96.7% cases and 70.9% of the lesions being smaller than 2 cm. Only 3.2% of the cases had diffuse swelling. Pain was an association in 12.9% of the cases.

Only 8.0% had the history of smoking/ tobacco chewing. One case (1.6%) had a previous history of squamous cell carcinoma of the maxilla.

Radiological investigations were available in 18 cases out of which majority (94.4%) had a solid lesion and only 5.5% of the lesions were cystic. No complex lesion was encountered.

Table 8: Cytological spectrum of cases in MSRSGC category II.

Cytological features	Cytological diagnosis	**Total no of cases (n-62)**	%
Acute inflammatory infiltrate + salivary gland acinar and ductal epithelial cells	Acute sialadenitis	**12**	19.4%
Chronic inflammatory infiltrate + ductal epithelial cells +/- salivary gland acinar cells	Chronic sialadenitis	**25**	40.3%
Epithelioid cell granulomas + chronic inflammatory infiltrate + salivary gland acinar + ductal epithelial cells +/- acute inflammatory infiltrate	Granulomatous sialadenitis	**3**	4.9%
Numerous salivary gland acinar cells + occasional ductal epithelial cells + stripped nuclei	Sialadenosis	**9**	14.5%
Scantily cellular smears + fluidy background +ductal epithelial cells	Non neoplastic cyst	**11**	17.7%
Reactive lymphoid population along with germinal center.	Reactive hyperplasia – Intra-parotid lymph node.	**1**	1.6%
Ductal epithelial cells + acinar cells +/- acute and chronic inflammatory cells	Others	**1**	1.6%

Under the non-neoplastic category, inflammatory etiology was seen to be

the most frequent with 19.4%, 40.3% and 4.9% of the cases categorized as chronic sialadenitis, acute sialadenitis, and granulomatous sialadenitis respectively. Most of the patients with inflammatory etiology had a tender swelling. Diabetes Mellitus was seen as a co-morbidity mainly in patients categorized as inflammatory etiology seen in 6.4% of the cases. Swelling was bilateral in 2 cases of granulomatous sialadenitis and 2 cases of sialadenosis.

In granulomatous sialadenitis no foci of necrosis was seen. 20% ZN stain for AFB in all these cases was non contributary. On clinical correlation these were found to be immune mediated granulomatous response – Sarcoidosis. One of the case was given the broad diagnosis of non-neoplastic lesion the cytology of which revealed mainly ductal epithelial cells with few clusters of acinar cells in a background containing red blood cells and few inflammatory cells. (Table 8)

Surgical biopsy was received in 5 cases and cell blocks were made in the 2 cases which were adequate.

Table 9: Cyto-histopathological correlation of cases in MSRSGC category II.

Cytological diagnosis	Histopathology (Surgical specimens/ cell blocks)		ROM
	Total no of cases	Diagnosis	
Chronic sialadenitis	3	Chronic sialadenitis	14.2%
Acute sialadenitis	1	Acute sialadenitis	
Nonneoplastic	1 1	Warthin's tumor Non neoplastic	
Reactive hyperplasia	1	Non hodgkins lymphoma	

Cyto-histopathological concordance in MSRSGC category II was noted to be 71.5%. Discordance was seen in 2 of the cases (28.5%) which was given the broad diagnosis of non-neoplastic on cytology showing reactive lymphoid cell population with occasional oncocytes and scanty epithelial cells which turned out to be Warthin's tumor on histopathology. Another case which was given the diagnosis of reactive hyperplasia turned out be Non hodgkins lymphoma on biopsy. The cause of misdiagnosis was attributed because of the large reactive lymphoid cell population with minimal number of atypical cells.

MSRSGC Category III – Atypia of undetermined significance. (AUS) [n-15 (9.4%)]

Aspirations that lack either quantitative or qualitative cytomorphologic features to be diagnosed with confidence as nonneoplastic or neoplastic were put under this category.

A total of 15 (9.4%) cases were classified under the Category III. The mean age was found to be 49.2 years with youngest being 13 years old and eldest being 75 years old. M:F ratio was found to be 2:1. Of the total cases, only 13.3% had the history of smoking/ tobacco chewing.

All the cases involved major salivary glands with parotid gland being the most common site (73.3%).

Majority (86.6%) had a lesion size less than 2 cm in diameter. All the lesions presented as unilateral swellings without association with pain/exaggeration while eating. In 86.6% of cases, the swellings were well circumscribed. Twenty percent of the lesions were mobile. Radiological findings were available in 6 cases of which 50% had a solid lesion, 33.3% had a cystic lesion while 16.7% had a complex lesion comprising of both solid and cystic components.

The smears showing proteinaceous to mucoid background containing inflammatory cells with few/ occasional clusters of vacuolated/ oncocytoid cells along with reactive atypia were classified as AUS- cystic lesion. The

cytological findings of all these lesions were analyzed in detail.

Table 10: Cyto-morphological features of cases in MSRSGC category III (n-15).

Cyto-morphological features	No of cases	%
Low cellularity	3	20%
Lymphoid cells	7	46.6%
Squamous cells	1	6.6%
Oncocytic cells	5	33.3%
Atypical/Vacuolated cells	4	26.6%
Reactive atypia	2	13.3%
Mucinous background	5	33.3%

Note: More than one feature were found in many of the cases.

Presence of lymphoid cells was the most common finding found in 46.6% of cases followed by oncocytic cells and mucinous background equally distributed among the cases (5 cases each) accounting for 33.3% each. Atypical cells/Vacuolated cells were found in 4 cases, reactive atypia was found in 2 cases (26.6%). While squamous cells were found in just one case (Table 10).

Surgical biopsy was received in 4 cases and cell blocks were made in the 9 cases which were adequate in 5 of the cases.

Table 11: Cyto-histopathological correlation of cases in MSRSGC category III (n-9).

Cytological diagnosis	Histopathology (Surgical biopsies and cell blocks)		ROM
	Total no of cases	Diagnosis	
AUS- Cystic lesion	2	Warthin's Tumor (both cases)	11.1%
AUS	7	1.Warthins tumor (2 cases) 2. Hodgkin's lymphoma (1 case) 3. AUS (4 cases)	

A definite histopathological diagnosis was available in 9 cases of which 5 were rendered neoplastic under which 4 were diagnosed as Warthin's tumor and one as Hodgkins lymphoma.

Of the lesions diagnosed as Warthin's tumor on histopathology, aspiration smears were scantily cellular and composed mainly of dirty proteinaceous background amidst which were scattered lymphoid cells and occasional oncocytic cells. The case diagnosed as Hodgkin's lymphoma showed reactive lymphoid cell population mainly with few atypical cells which could not be further categorized on cytology.

In 4 of the cases the findings of all the cell blocks were similar to those on the smears and hence no histopathological diagnosis could not be made, while in four cases cell blocks were rendered inadequate for opinion. (Table 11)

MSRSGC Category IV – Neoplastic [n-67 (42.8%)]

A total of 67 cases were diagnosed as category IV – Neoplastic, of which 57 cases were subcategorized as benign and 10 cases as SUMP.

A named entity was given to all the cases in the Benign category (IV a).

Neoplasm: Benign Category [n-57 (35.6%)]

Aspirations that showed characteristic cytomorphological features of a specific benign epithelial or mesenchymal neoplasm of salivary gland were put under the benign category.

A total of 57 cases were categorized into neoplastic – benign. The mean age was found to be 48.8 years with youngest being 15 years old and eldest being 84 years old. M:F ratio was found to be 1.1:1

Majority of the cases under the subcategory benign had a lesion in the major salivary glands with parotid gland being the most common site. Seven percent of the cases had lesions in the minor salivary glands all of which were seen as palatal lesions.

All the cases had a well circumscribed swelling and 50% of the lesions had size more than 2 cm in diameter. Of the total cases in this category, 94.7% had a unilateral lesion and 1.7% of the patients had an association with pain.

Only 7.0% had history of smoking/ tobacco chewing of which 3 cases were diagnosed as Warthin's tumor. Three cases (5.2%) had a previous history of carcinoma and were undergoing adjuvant chemo/radiotherapy. (Two patients had previous history of breast carcinoma and 1 had lung carcinoma.)

Radiological findings were available in 17 cases, out of which majority had a solid lesion (94.1%) while only 5.8% of the cases with a complex lesion having both solid and a cystic component.

Table 12: Cytological spectrum of cases in MSRSGC category IV a- Benign according to cytological diagnosis (n-57).

Cytological features	Cytological diagnosis	**Total no of cases (n-57)**	%
Chondromyxoid stroma +bland epithelial and myoepithelial cell clusters	Pleomorphic adenoma	**38**	66.7%
Oncocytic cell clusters + reactive lymphoid cells + granular debris +/- mucoid background	Warthins Tumor	**19**	33.3%

The most common diagnosis on cytopathology was found to be Pleomorphic adenoma (66.7%) followed by Warthin's tumor (33.3%) (Table 12)

Table 13: Cyto- histological correlation of cases in MSRSGC category. IV- Benign.

Cytological diagnosis	Histopathology (surgical biopsy and cell blocks)		Risk of malignancy
	No of cases (n-26)	Diagnosis	
Pleomorphic adenoma	**8** **1** **1** **1**	Pleomorphic Adenoma Myoepithelioma Mucoepidermoid carcinoma Nodular fascitis	11.6%
Warthin's tumors	**13** **1** **1**	Warthins tumor Mucoepidermoid carcinoma Acinic cell carcinoma	

Surgical biopsy was available for 13 cases and cell blocks were made in 14 cases which were adequate.

Histopathological diagnosis was available for 26 cases. Cyto-histological agreement for the benign category was achieved in 23 out of 26 cases (88.4%) while accuracy of benign neoplastic diagnosis was 91.3%. Discordant cases were found to be 3 out of 26 cases (11.6%).

The case diagnosed as Acinic cell carcinoma on histopathology had metastatic deposits of the carcinoma in the intra-parotid lymph node, the cytology smears of the same had a dense lymphoid cell population with clusters cells appearing to have oncocytic cytoplasm which led to the diagnosis of Warthin's tumor on cytology.

Another 2 cases diagnosed as mucoepidermoid carcinoma on histopathology had mucoid background with limited number of overtly malignant cells in the cytology smears that led to the discordance. Overall risk of malignancy was found to be 11.6% (Table 13)

Neoplasm: Salivary gland tumor of uncertain malignant potential. (SUMP) [n-10 (6.2%)]

This diagnostic category was reserved for aspirations that were diagnostic of a neoplasm however, a definitive diagnosis of a specific entity couldn't be made.

A total of 10 cases were diagnosed as SUMP with a mean age of 52.2 years with youngest patient being 37 years old and eldest being 70 years old. The M:F ratio was found to be 0.4:1

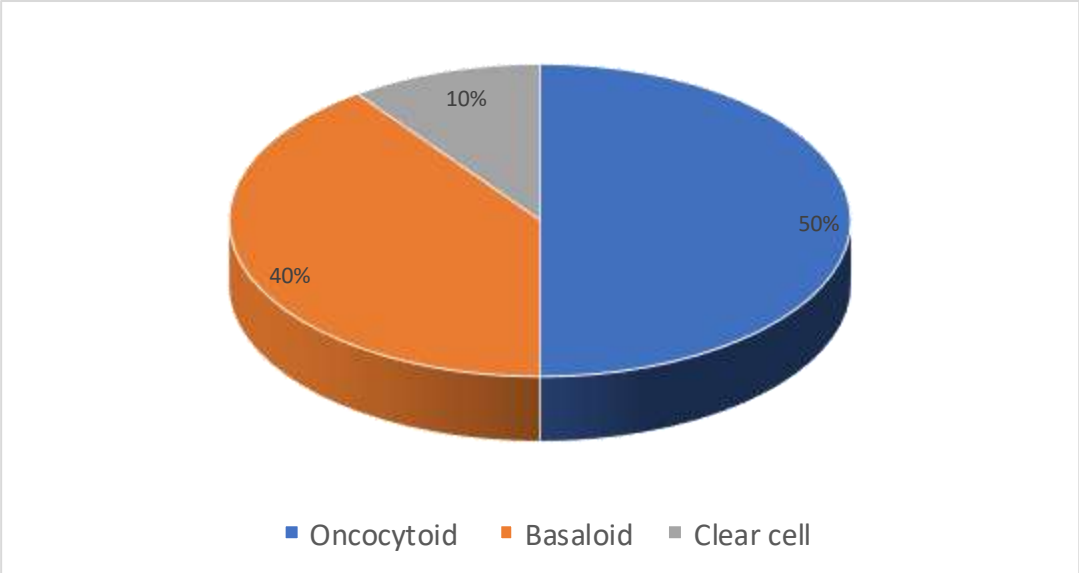
Ninety percent of the cases had a lesion in the major salivary glands with parotid gland being the most common site. One of the cases had a lesion in the minor salivary gland in the oral cavity being the most common site accounting for 10% of the cases.

Seventy percent of the cases had a lesion of the size less than 2 cm in diameter. All the lesions were found to be unilateral. Swelling was the most common presenting symptom seen in all the cases of which well

circumscribed swelling was found to be in 90% of the cases and 10% of the cases had a tender swelling. History of smoking/ tobacco chewing was found in 10% of the cases. None of the patients had any co- morbidities. Radiological findings were available for 3 cases of which all had a solid lesion.

The lesions under the SUMP category were further divided on the basis of cytological features of the smear into basaloid, oncocytoid and clear cell types. Of the total cases, 50% of the lesions had cells with oncocytoid morphology i.e. cells with well-defined boundaries and abundant amount of granular cytoplasm and 40% had basaloid morphology i.e. the cells with a round nuclei and scant amount of cytoplasm and 10% of the cases had clear cell type morphology having clear cytoplasm. (Chart 3)

Fig. 3: Cytomorphological spectrum of cases classified as Neoplasm: SUMP.



Surgical biopsy was available for 1 case and cell blocks were made in 5 cases which were adequate

Table 14: Cyto- histological correlation of cases in MSRSGC category IV- SUMP.

Cytological diagnosis	Histopathology (surgical biopsies and cell blocks)		ROM
	No of cases	Histopathological diagnosis	
SUMP	1 1	Myoepithelioma Warthin's tumor	0%

Cyto-histopathology correlation of cases in MSRSGC category IV was available for 6 cases of which one was diagnosed as myoepithelioma and other was rendered the diagnosis of warthin's tumor. In the remaining 4 cases, sections from the cell blocks had features similar to their cytopathology smears hence a definitive diagnosis could not be reached.

The cytology of myoepithelioma revealed papillaroid configuration, micro-acini and singly dissociated cells with altered N:C ratio with focal membrane irregularity and cytoplasmic vacuolation. Many of the cells with extracellular stromal material was seen present against a mucoid background. The differential diagnosis on cytology were kept as Pleomorphic adenoma, Myoepithelioma and Epithelial- Myoepithelial carcinoma The histopathology of the same showed a well encapsulated tumor arranged in nests with cells having vesicular nuclei and moderate cytoplasm embedded in a hyaline stroma. The presence of extra cellular stromal material with atypical changes of the cells were the factors that favored the cytological diagnosis of SUMP.

Another case diagnosed as SUMP with oncocytic features was reported as Warthin's tumor on histopathology showed limited number of oncocytic clusters with presence of a large population of reactive lymphocytes with in a mucinous background which were limiting factors in diagnosing the

case as SUMP.

MSRSGC Category V - Suspicious for malignancy [n-2 (1.2%)]

An aspirate was considered to be suspicious for malignancy when some, but not all the criteria for a specific diagnosis of malignancy were present but the overall cytologic features were suggestive of malignancy.

In our study 2 cases were categorized into this category. Both the patients were males, smokers in 6^{th} and 8^{th} decade of life, had a circumscribed, immobile and unilateral swelling in the parotid gland and submandibular gland respectively. The size of the parotid swelling was 1cm in diameter. On histopathology it was diagnosed as a benign tumor- Warthin's tumor. The other was in the submandibular gland with a lesion of 5cm and the radiology was suggestive of a solid lesion. The patient expired because of the widespread metastasis and no histopathology was available. Risk of malignancy was accounted to be 50% for this category.

MSRSGC Category VI – Malignant [n-7 (4.4%)]

Aspirations with cytomorphological features that either alone or in combination with ancillary studies were diagnostic of malignancy were put under this category.

A total of 7 cases were categorized as Malignant with mean age of 54.8 years with youngest being 11 years old and eldest being 88 years old. M:F ratio was found to be 0.3:1

Most common site of lesion was found to be in major salivary gland with parotid being the most commonly affected gland (42.8%). One case affecting the minor salivary glands was seen as palatal swelling.

Seventy one percent of the cases had a lesion of size less than 2cm. All the patients presented with a unilateral and well circumscribed swelling. Association with pain was found in 28.5% of the cases.

2 cases were follow-up cases of adenoid cystic carcinoma and one case of Muco-epidermoid carcinoma

Radiological findings were available for 5 cases all of which were reported to be solid lesions. Surgical biopsy was available in all the seven cases.

Table 15: Cytological spectrum of cases in MSRSGC category VI (n-7).

Cytological features	Cytological diagnosis	**Total no of cases**	%
Hyaline globules + embedded atypical basaloid cells	Adenoid cystic carcinoma	**03**	42.8%
Intermediate cells + squamoid cells + vacuolated cells + dirty mucinous background.	Muco-epider moid carcinoma	**02**	28.6%
Overtly malignant cells with altered N:C ratio +Atypical mitosis +Atypical squamoid cells +/- necrosis	Malignant aspirate - NOS	**02**	28.6%

Adenoid cystic carcinoma was found to be the most common malignancy found in 3 out 7 cases. 2 of the cases no special type could be ascertained and hence left at malignant aspirate NOS (Table 15)

Table 16: Cyto-histological correlation of cases in MSRSGC category VI (n-7).

Cytological diagnosis	Histopathology		Concordance	ROM
	No of cases	Diagnosis		
Adenoid cystic carcinoma	**3**	Adenoid cystic carcinoma	100%	100%
Mucoepidermoid carcinoma	**2**	Mucoepidermoid carcinoma	100%	
Malignant aspirate	**2**	1.Metastatic Squamous cell carcinoma 2. Salivary duct carcinoma	100%	

Of the total malignant cases, 6 cases were of primary salivary gland tumors.

Of which 50.0% were diagnosed as adenoid cystic carcinoma, 33.3% were diagnosed as mucoepidermoid carcinoma. While the rest 2 case which were categorized malignant aspirate on cytology were diagnosed as of Squamous cell carcinoma and Salivary duct carcinoma on histopathology. Risk of malignancy and concordance was found to be 100%. (Table 16)

A total of 10 cases were found to be discordant, the summary of which is described below in the table. (Table 17)

Table 17: Summary of discordant cases according to MSRSGC category.

Category	Cytological findings	Surgical diagnosis
II	Reactive lymphoid cells with scanty oncocytes and epithelial cells - Non-neoplastic	Warthin's tumor
II	Reactive lymphoid cell population – Reactive hyperplasia, intraparotid lymph node	Non hodgkins lymphoma
III	Reactive lymphoid cells with occasional atypical cell - intraparotid lymph node	Hodgkin's lymphoma
III	Scantily cellular aspiration with scattered lymphoid cells and occasional oncocytes.	Warthin's tumor
IV a	Cells with plasmacytoid morphology present in a myxoid stroma – Pleomorphic adenoma	Mucoepidermoid carcinoma
IV a	Cells with eccentric nuclei and abundant cytoplasm present in a dirty granular backround containing reactive lymphoid cells – warthins tumor	Mucoepidermoid carcinoma
IV a	Dense lymphoid infiltrate with few cells showing having centrally placed nuclei and abundant cytoplasm present in a dirty background - Warthins tumor	Acinic cell carcinoma with metastasis to the intraparotid lymph node.
V	Atypical cells with mild nuclear pleomorphism present in a necro-inflammatory background. -Suspicious for malignancy	Warthin's tumor

Warthin’s tumor was the most frequently misinterpreted lesion in our study accounting for 14.3% of the cases.

DISCUSSION

The establishment of MSRSGC for reporting salivary gland FNA represents an essential step towards standardizing terminology and hence improving the overall effectiveness of salivary gland FNA and improved patient care. The MSRSGC is a six tier international classification scheme with risk stratification comprising of Category I- Non diagnostic, Category II – Non neoplastic, Category III- Atypia of undetermined significance (AUS), Category IV- Neoplastic which is subcategorized as Benign (IV a) and SUMP (IV b), Category V- Suspicious for malignancy and Category VI- Malignant

Table 18: Category wise distribution of cases in various studies.

Category	Present study	Chayanika et al [35]	Vishwanathan K et al [11]	Thiryayi et al [32]	Howard H Wu et al [37]	Jaslyn jie lin lee et al [38]
	n=160	n=293	n=627	n=272	n=1560	n=1384
I	4.3%	6.1%	12%	21.3%	18.8%	28.9%
II	38.7%	38.2%	28.5%	22%	21.5%	18.0%
III	9.3%	2.7%	6.1%	2.4%	3.8%	9.8%
IVa	35.6%	33.4%	31.4%	36.9%	37.2%	32.9%
IVb	6.2%	2.0%	9.9%	5.2%	5.9%	5.7%
V	1.2%	2.4%	2.7%	1.7%	1.2%	1.6%
VI	4.3%	15%	9.4%	10.5%	11.4%	3.2%

In the present study, the cytological categorization of 160 cases according to MSRSGC was done. In the current study Category IV (Neoplastic) was the most common category comprising of 41.8% of the cases of which most of the cases were subcategorized as Benign. This was followed by Category II (Nonneoplastic) comprising of 38.7% of the cases. As shown

in Table No 18 this was corroborated by many authors like Vishwanathan et al,[11] Thirayi et al[32] Howard H Wu et al[37] and Jaslyn jie lin[38] et al in their respective studies. Neoplasms were the commonest lesions of salivary gland in both Indian as well as international studies. In contradiction to these findings, Chayanika et al [35] in her study of 293 cases showed maximum number of cases in Category II.

Age and sex prevalence

In our study, the age of the patients ranged from 6 years to 88 years with the highest number of patients in the age group of 41-60 years (42.8%) and mean age of 49.4 years. Slightly more males (53.7%) were affected as compared to females (46.3%) thus we found M:F ratio of 1.1:1. This finding was found to be concordant with that of Jaslyn Jie Lin Lee et al[38] who reported the mean age of patients as 50.1 years and M:F ratio of 1.5:1. Another study by K Amita et al[39] showed the mean age of patient was 48.3 years with youngest patient being 9 years old and oldest being 83 years old and M:F ratio 2.1:1. In a study conducted by Charlotte et al[40] the mean age of patients was slightly higher than in our study i.e. 64 years with youngest being 11 years old and eldest being 93 years old and the M:F ratio 1:1.1 Better social status of females and ease of access to health care may have be responsible for an almost equivalent gender ratio and wider age distribution.

Clinical presentation of the cases

The lesions were analysed according to the clinical presentation including symptom, signs, co-morbidities and imaging studies.

In our study, major salivary glands were more frequently involved with lesions distributed among all the categories however minor salivary glands were found to be involved only by lesions of the neoplastic categories (category IV, V and VI). Parotid gland was the most common salivary gland involved followed by submandibular gland. These were found to be concordant with the studies conducted by Ritu jain et al[31], Vaishali P Gaikwad et al[41], and Jalal et al[42], who found major salivary gland was

frequently involved with parotid gland being most commonly affected (67.5%, 68.3%,71.6% respectively) and minor salivary gland being affected in only 2.5%,1.9% and 3.8% of the lesions.

In the present study the size of lesions varied from 0.5 cm to 7.0 cm, with majority of lesions (67.5%) measuring less than 2 cm while just 1.8% of lesions were found to have size more than 5 cm. These findings were found concordant with the studies conducted by K Vishwanathan et al[11] and Erkka tammola et al.[34] They found the size of the lesions to be in the range of 0.2 -10.0 cm with an average size of around 2 cm.

The lesions were predominantly unilateral, constituting 96.2% of the total cases. The salivary gland swelling was present in all the cases, which were well circumscribed swelling was found in 96.8% of the cases, and mobile swelling in 3.7% of the cases. Swellings were painful in 6.8% of the cases, majority of which were classified under inflammatory category. This was found to be concordant with the study conducted by Young A et al [43]who noted that majority of the salivary gland lesions presented with a painless, well circumscribed swelling.

MSRSGC Category I - Non-Diagnostic [n=7, (4.4%)]

In the present study, 4.3% of cases were categorized under the Non-diagnostic category. All the swellings were present in the major salivary glands. These were found to be concordant with the studies conducted by Jaslyn Jie Lin Lee et al.[38] they found the parotid gland to be the most common site. Out of all non-diagnostic cases of our study, 85.7% of cases had scanty cellularity while 14.2% of the cases had only blood in the smears with insufficient epithelial cell elements/ matrix components/inflammatory cells/cyst fluid hence making the slides non diagnostic for evaluation. These findings were found to be concordant with studies conducted by Thiryayi et al[31], Ritu jain et al[32] and Deepika Sawant et al[36] where low cellularity, small size of the lesion and hemorrhage were the major reasons for non-diagnostic cases.

As no biopsy was received and cell blocks made were inadequate so cyto-histopathological correlation or risk of malignancy could not be deduced for this category.

MSRSGC Category II - Non neoplastic [n- 62(38.8%)]

Under the non-neoplastic category, inflammatory etiology was seen to be the most frequent with cases categorized as chronic sialadenitis, acute sialadenitis, and granulomatous sialadenitis. These findings were found to be concordant with studies conducted by Malathi et al[44] and Hafeez et al. [45,] The study conducted by Das et al[46] also had the similar findings. They found the most common diagnosis to be inflammatory pathology with chronic sialadenitis as the most common diagnosis under the non-neoplastic category in their studies.

Cyto-histopathological concordance in MSRSGC category II was noted to be 83.3%. Discordance was seen in 2 of the cases (16.7%), in one of which Warthin's tumor could just be given a broad diagnosis of non-neoplastic on cytology because of predominance of reactive lymphoid cell population and lack of oncocytes and even epithelial cells. In another case Non Hodgkin lymphoma was diagnosed as reactive lymphoid hyperplasia on aspiration. Jaiswal P et al [47] and Tyagi et al [48] in their studies also misdiagnosed Warthins tumor and Non Hodgkins lymphoma as non-neoplastic lesions. The reactive lymphoid population with occasional oncocytes was found to be the cause of misdiagnosis in the first case. In the second case the presence of reactive immunoblasts within a reactive lymphoid population was the cause of misdiagnosis. Charlotte et al[40] in their study also misdiagnosed a non-neoplastic lesion as Warthins tumor. Thus the cause of misdiagnosis was found similar with our study.

The risk of malignancy was found to be 14.2% in our study which was within the range set by MSRSGC (10-20%). The ROM in our study was slightly higher than the study conducted by Nesreen et al [45] where the

ROM was found to be 11.8% while in another study conducted by Jaiswal et al[47] the ROM was found to be 7.14%. The higher ROM in our study is attributed due to a smaller sample size than other studies.

MSRSGC Category III – Atypia of undetermined significance. (AUS) [n-15 (9.4%)]

Aspirations that lack either quantitative or qualitative cytomorphologic features to be diagnosed with confidence as nonneoplastic or neoplastic were put under this category.

A total of 15 (9.4%) cases were classified under the Category III which were within the brackets set by MSRSGC. Sintawat et al [49] and Maria rivera et al [50] had also put 4.8 % and 4.3% cases in this category in their studies respectively.

The smears showing proteinaceous to mucoid background containing inflammatory cells with few/ occasional clusters of vacuolated/ oncocytoid cells along with reactive atypia were classified as AUS- cystic lesion. Maleki et al [30] and pantnowitz et al [51] in their studies also included those cases under AUS which consisted of abundant mucin with or without rare epithelial cells or specimens with rare atypical cells where a malignant neoplasm could not be ruled out.

Horward H wu et al [37] in their study noted that cases that that were put under the AUS category had a prominent lymphoid component. They also noted that reactive lymph nodes can occasionally have increased proportions of larger cells which can lead to the diagnosis of AUS and most of them represented lymphomas, reactive lymph nodes, or sialadenitis on histopathology. This was found to be concordant to our study too as presence of lymphoid cells was the most common finding found in 7 out of total 15 cases. A definite histopathological diagnosis was available in 9 cases of which 5 were rendered neoplastic under which 4 were diagnosed as Warthin's tumor and one as Hodgkins lymphoma.

On analysis of the lesions diagnosed as Warthin's tumor on

histopathology in the category III, aspiration smears were scantily cellular and composed mainly of dirty proteinaceous background amidst which were scattered lymphoid cells and occasional oncocytic cells which were thought be metaplastic in origin. The case diagnosed as Hodgkin's lymphoma showed reactive lymphoid cell population mainly with few atypical cells which could not be further categorized on cytology. These was found to be concordant with the studies conducted by Sintawat et al, [37] Horward H Wu et al [49] and Maria Rivera et al [50] where the most common reason to classify an aspirate containing lymphocytes as AUS was a lack of a monomorphic population as well as the presence of only rare atypical lymphocytes. Diagnosis of Warthins tumor on aspiration was deferred and put under AUS when any one or two things amongst oncocytes, lymphoid cells, and a "dirty" proteinaceous background were found to be missing.

ROM in our study was found to be 11.1% which is within the range set by MSRSGC [10-35%] which was found to be concordant with studies like that of Deepika et al [36] who found ROM to be 20% in their study. [52]

MSRSGC Category IV – Neoplastic: Benign Category [n=57(35.6%]

Aspirations (35.6% cases, N=57) that showed characteristic cytomorphological features of a specific benign epithelial or mesenchymal neoplasm of salivary gland were classified under the benign category.

Majority of the cases under the subcategory benign had a lesion in the major salivary glands with parotid gland being the most common site. Seven percent of the cases had lesions in the minor salivary glands. These findings were consistent with study conducted by Samoon Nuzhat et al[53] Doh Young Lee et al[54] and Dandapat et al[55] who found parotid gland to be the most common site for this category.

The most common diagnosis on cytopathology was found to be Pleomorphic adenoma. These findings were consistent with those of Simon Sung et al[56] and Manucha et al. [57] They found the most common

tumor in the benign category as Pleomorphic adenoma.

Cyto-histological agreement for the benign category was achieved in 23 out of 26 cases (88.4%); thus accuracy of benign neoplastic diagnosis was 91.3%. Discordant cases were found to be 3 out of 26 cases (11.6%). One case diagnosed as warthins tumor on cytology was diagnosed as Acinic cell carcinoma with metastasis in intraparotid lymph node on histopathology. On reviewing the cytology smears of the same had a dense lymphoid cell population with clusters of granular cells mistaken as oncocytes which led to the diagnosis of Warthin's tumor on cytology. In studies conducted by Doh Young Lee et al[54] and Hughes et al[58] the most common reason for an aspiration smears to be misdiagnosed as acinic cell carcinoma was because of scarcity of matrix material with a dominant epithelioid or myoepithelial cell component. Acinic cell carcinoma was found to be a common differential of Warthins tumor in their study as well.

Another two cases which were misdiagnosed as Pleomorphic adenoma and Warthins tumor on cytology were later diagnosed as Mucoepidermoid carcinoma on histopathology. Presence of mucoid background with limited number of overtly malignant cells in the cytology smears that led to the discordance. These finding were also found in the study conducted by Nasreen H hafiz et al. [45] Cyst fluid aspiration with only mucinous background with scattered lymphocytes and rare mucus cells may cause this underdiagnosis. Another study by Deepika et al[36] noted that smears that were paucicellular with few sheets of epithelial cells in a background of lymphocytes, macrophages and abundant mucinous material were confused with benign neoplasms such as pleomorphic adenoma.

Overall risk of malignancy was found to be 11.6% in our study which was found to be within the range set by MSRSGC (i.e. 0-13%). Our value was slightly more than findings by Rohilla et al,[33] Griffith et al[59] and Chayanika et al[35] where the ROM was 7.3% and 4.4% respectively only. The higher ROM in our study may be because of low sample size.

Neoplasm: Salivary gland tumor of uncertain malignant potential. (SUMP) [n=10(6.2%)]

The lesions under the SUMP category [n-10 (6.2%)] were further divided on the basis of cytological features of the smear into oncocytoid morphology i.e. cells with well-defined boundaries and abundant amount of granular cytoplasm, basaloid morphology i.e. the cells with a round nuclei and scant amount of cytoplasm and of the cases had clear cell type morphology having clear cytoplasm.

Cyto-histopathology correlation of cases in MSRSGC category IV was available for 6 cases of which one was diagnosed as Myoepithelioma and other was rendered the diagnosis of Warthin's tumor. In the remaining 4 cases, sections from the cell blocks had features similar to their cytopathology smears hence a definitive diagnosis could not be reached.

The cytology of Myoepithelioma revealed papillaroid configuration, micro-acini and singly dissociated cells with altered N:C ratio with focal membrane irregularity and cytoplasmic vacuolation. Many of the cells with extracellular stromal material was seen present against a mucoid background. The differential diagnosis on cytology were kept as Pleomorphic adenoma, Myoepithelioma and Epithelial - Myoepithelial carcinoma. The histopathology of the same showed a well encapsulated tumor arranged in nests with cells having vesicular nuclei and moderate cytoplasm embedded in a hyaline stroma. The presence of extra cellular stromal material with atypical changes of the cells were the factors that favored the cytological diagnosis of SUMP.

Hang et al[60] noted in their study that presence of extracellular matrix are nonspecific for the diagnosis and are misleading. Presence of hyaline globules surrounded by basaloid cells are seen in adenoid cystic carcinoma, benign basal cell adenoma, pleomorphic adenoma, and myoepithelioma, and thus leading to false-positive diagnoses, hence many lesions need to be kept under the SUMP category. Liu H et al [61] in their study found that differentiating between benign and malignant tumors with

basaloid features a diagnostic challenge and noted that many a times it is impossible because of overlapping cytomorphology. It was also noted that the tumours with myoepithelial differentiation exhibit indeterminate atypical features with focal questionable atypia, present in cases that otherwise exhibit characteristic features of pleomorphic adenoma which maybe the part of the carcinomas that occasionally may arise from pleomorphic adenomas and exhibit aggressive behaviour hence were kept under the SUMP category. They found it challenging to distinguish between a benign and a bland-looking, low-grade to intermediate-grade malignant tumor because of cytomorphologic overlap and diversity. [62, 63]

Another case diagnosed as SUMP with oncocytic features was reported as Warthin's tumor on histopathology showed limited number of oncocytic cell clusters with presence of a large population of reactive lymphocytes within a mucinous background which were limiting factors in definite diagnosis and led to diagnosing the case as SUMP. Manucha et al[57] noted in their study that Warthin tumor was difficult to differentiate from a mucoepidermoid carcinoma, acinic cell carcinoma, and even a squamous cell carcinoma hence the suspicious smears were cautiously kept under the SUMP category. Another study by Hafez et al[45] found that suspicious epithelial cells with squamoid morphology, likely oncocytic epithelium undergoing squamous metaplasia with a dirty background can cause an over-diagnosis leading to categorization of such smears in SUMP.

ROM in our study was found to be 0% which was lower than in various other studies where ROM of 35% and 34.2% was found. [11, 35] Lower ROM in our study is because of the smaller sample size and as biopsy specimens were not available for all the cases.

MSRSGC Category V - Suspicious for malignancy [n-2 (1.2%)]

An aspirate was considered to be suspicious for malignancy when some, but not all the criteria for a specific diagnosis of malignancy were present but the overall cytologic features were suggestive of malignancy.

In our study 2 cases were categorized into this category. On histopathology one was diagnosed as a benign tumor- Warthin's tumor. The other patient expired because of the widespread metastasis before a biopsy could be performed, hence and no histopathology was available. Malathi et al[44] noted in their study that Warthin tumor on cytology can cause increased false positive and false negativity due to sampling error like metaplastic squamous cells, only epithelial cells with cyst macrophages, and variable amount of lymphocytes hence making it difficult to be diagnosed. Another study by Maleki et al[50] concluded that scant cellularity of malignant cells, a necrotic or mucinous background, poor preservation of the aspirated material, and the presence of lymphocytes were reported in multiple cases contributed to the diagnosis of Suspicious for malignancy. These findings were similar to those in our study where the highly cellular smears reactive lymphoid population with metaplastic epithelial cells leading to the over diagnosis of suspicious for malignancy.

Risk of malignancy accounted to be 50% for this category which is concordant with the range set by MSRSGC (i.e. 0-100%). This finding is concordant with studies conducted by Chen et al, [64] Montezuma et al [65]and Wei S et al[66] where ROM was 60%, 50%, 58.6% respectively.

MSRSGC Category VI - Malignant [n=7(4.4%)]

Aspirations with cytomorphological features that either alone or in combination with ancillary studies were diagnostic of malignancy were put under this category.

Adenoid cystic carcinoma was found to be the most common malignancy followed by Mucoepidermoid carcinoma. While the rest 2 case which were categorized malignant aspirate on cytology were diagnosed as Squamous cell carcinoma and Salivary duct carcinoma on histopathology. The study conducted by Jaslyn lee et at [38] found Mucoepidermoid carcinoma to be the most common malignancy followed by adenoid cystic

carcinoma. Deepika et al[36] also found in their study mucoepidermoid carcinoma to be the most common carcinoma. Wang et al[67] in their stated that metastatic squamous cell carcinoma from all sites constituted the majority of secondary malignancies of salivary glands. the most common malignancy as Adenoid cystic carcinoma in our study is attributed because of the lower sample size. Risk of malignancy and concordance was found to be 100%. This was found to be similar to most of the studies including Nasreen et al[40] and charlotte et al[45] where the risk of malignancy was found to be 100 %.

In our study, Warthins tumor was found to be the most misinterpreted lesion which was due to the cystic nature of the lesion and procedural cause as many aspirations were performed without the radiological guidance. The cytology of the misdiagnosed lesions showed mainly extracellular mucin like material or lymphoid population with presence of occasional oncocytic cells. Maleki et al[50] noted in their study that overlapping features of benign and malignant cystic salivary gland conditions, the complexity of this anatomic site and the variable experience of the radiologist made the interpretation of the cystic lesions more challenging. They also commented that lymph nodes with involvement by metastatic carcinoma, lymphoma, or even reactive changes can mimic salivary gland cysts.

Salehi et al[68] in their study stated that Warthin tumors sometimes can be mistaken for malignancy in FNA specimens with various differential diagnosis including oncocytosis, oncocytoma, Warthin tumor, oncocytic carcinoma, pleomorphic adenoma, the oncocytic variant of mucoepidermoid carcinoma, acinic cell carcinoma, and metastatic renal cell carcinoma. Vishwanathan et al[11] in their study also brought forth presence of mucin-like extracellular material as a pitfall in diagnosing Warthins tumor.

SUMMARY & CONCLUSION

A study was conducted on salivary gland apirates of 160 patients who had undergone fine needle aspiration (FNA) by percutaneous method, ultrasound guided or CT guided method over a period of five years [three and a half years retrospectively (1st July 2015 to 31st December 2018) and one and half year prospectively (1st January 2019 to 30th June 2020)] conducted in Dayanand Medical College and hospital, Ludhiana.

In each patient, clinical and radiological findings were recorded. Correlation with histopathology was done wherever possible

Histopathological correlation was available in 52 cases.

The following conclusions were made:

1. Maximum cases were found to be in the age group of 41-60 years (42.8%). Mean age was found to be 49.46 years with youngest patient being 6 years old and oldest being 88 years old.
2. Slight male preponderance was seen with M:F ratio of 1.1:1
3. Swelling was the major presenting symptom (96.9% cases had a well circumscribed swelling).
4. Parotid gland was the most commonly involved gland (68.12% cases).
5. Bilateral swellings were found in 3.8% of the total cases which comprised of granulomatous sialadenitis, sialadenosis and Warthins tumor.
6. Direct percutaneous aspiration was more commonly employed technique
7. The lesions were categorized on cytology under the following categories: Non diagnostic (4.4%), Non neoplastic (38.8%), Atypia of undetermined significance (9.4%), Neoplastic- (41.8%), Suspicious for malignancy (1.2%) and Malignant (4.4%).
8. Neoplastic category comprised the greatest number of cases (41.8%) that were subcategorized further into benign category (35.6%) and SUMP (6.2%)

‘SUMP’ was further classified based on the cytological features as basaloid, oncocytoid and clear cell type. These comprised of 40%, 50% and 10% of the total cases under this subcategory. The ROM for this category was found to be 0%.

9. Non neoplastic cases constituted 38.8% of the total cases, under which the inflammatory etiology was seen to be the most frequent with 40.3%, 19.4% and 4.9% of the cases categorized as acute sialadenitis, chronic sialadenitis, and granulomatous sialadenitis respectively. ROM for this category was found to be 14.2%. Discordance was found to 28.5%.

10. The category Atypia of undetermined significance on cytology encompassed 9.4% of the cases which is an intermediate category for aspirations that lack either quantitative or qualitative cytomorphologic features to be diagnosed with confidence as nonneoplastic or neoplastic. ROM was found to be 11.1%

11. Suspicious for malignancy formed 1.2% of total cases which is also an intermediate category. ROM was found to be 50%

12. Non diagnostic accounted for 4.4% of cases which was due to poor cellularity and/or poor preservation of the aspirates.

13. Malignant category comprised 4.4% of the total cases out which adenoid cystic carcinoma was most commonly seen (42.8%). ROM was found to 100%

14. Warthin’s tumor was the most frequently misinterpreted lesion in our study accounting for 14.3% of the cases.

BIBLIOGRAPHY

1. Kessler AT, Bhatt AA. Review of the major and minor salivary glands, part 1: anatomy, infectious, and inflammatory processes. Journal of clinical imaging science. 2018;8:47.
2. Daneshbod Y, Daneshbod K, Khademi B. Diagnostic difficulties in the interpretation of fine needle aspirate samples in salivary lesions: Diagnostic pitfalls revisited. Acta Cytol. 2009;53(1):53-70.
3. Seethala RR, LiVolsi VA, Baloch ZW. Relative accuracy of fine-needle aspiration and frozen section in the diagnosis of lesions of the parotid gland. Head Neck. 2005;27(3):217-23.
4. Layfield LJ, Baloch ZW, Hirschowitz SL, Rossi ED. Impact on clinical follow-up of the Milan System for salivary gland cytology: A comparison with a traditional diagnostic classification. Cytopathology. 2018;29(4):335-42.
5. Solomon D, Davey D, Kurman R, Moriarty A, O'Connor D, Prey M, et al. The 2001 Bethesda System: terminology for reporting results of cervical cytology. JAMA. 2002;287(16):2114-9.
6. Kline TS, Merriam JM, Shapshay SM. Aspiration biopsy cytology of the salivary gland. Am J Clin Pathol.1981;76(3):263-9.
7. Rossi ED, Wong LQ, Bizzarro T, Petrone G, Mule A, Fadda G, et al. The impact of FNAC in the management of salivary gland lesions: Institutional experiences leading to a risk based classification scheme. Cancer Cytopathol. 2016;124:388-96.
8. Rossi ED, Faquin WC, Baloch Z, Barkan GA, Foschini MP, Pusztaszeri M, et al. The Milan System for Reporting Salivary Gland Cytopathology: Analysis and suggestions of initial survey. Cancer. 2017;125(10):757-66.
9. Nayar R, Wilbur DC. The Pap test and Bethesda 2014. Cancer Cytopathol. 2015;123(5)-271-81.

10. Ali SZ, Cibas E. The Bethesda System for Reporting Thyroid Cytopathology: Definitions, Criteria and Explanatory Notes. 1st ed. New York: Springer US; 2010.
11. Viswanathan K, Sung S, Scognamiglio T, Yang GC, Siddiqui MT, Rao RA. The role of the Milan System for Reporting Salivary Gland Cytopathology: A 5-year institutional experience. Cancer Cytopathol. 2018;126(8):541-51.
12. Foschini MP, Rossi ED, Higuchi K, Jhala NC, Kholová I, Urano M, et al. Non-Diagnostic. In The Milan system for reporting Salivary Gland cytopathology. Switzerland: Springer; 2018. pp. 11-20.
13. Faquin WC,, Bongiovanni M, Callegari FM, Canberk S, Elsheikh TM, Kurtycz DFI et al. Non-Neoplastic. The Milan system for reporting Salivary Gland cytopathology. Switzerland: Springer; 2018. pp. 21-42.
14. Pusztaszeri M, Baloch Z, Faquin WC, Rossi ED, Tabatabai ZL. Atypia of Undetermined Significance. The Milan system for reporting Salivary Gland cytopathology. Switzerland: Springer; 2018. pp. 43-54.
15. Baloch Z, Fadda G, Fırat P, Klijanienko J, Krane JF, Layfield L, et al. Neoplasm. The Milan system for reporting Salivary Gland cytopathology. Switzerland: Springer; 2018. pp. 55-84.
16. Mazzola F, Tomasoni M, Mocellin D, Dalè M, Iandelli A, Carobbio A, Marchi F, et al. A multicenter validation of the revised version of the Milan system for reporting salivary gland cytology (MSRSGC). Oral Oncology. 2020;109:104867.
17. Eneroth CM, Jakobsson P, Zajicek J. Aspiration biopsy of salivary gland tumors. V. Morphologic investigations on smears and histologic sections of acinic cell carcinoma. Acta Radiol Suppl. 1971;310:85–93.
18. Brandwein MS, Huvos AG. Oncocytic tumors of major salivary glands. A study of 68 cases with follow-up of 44 patients. Am J Surg Pathol. 1991;15(6):514–28.

19. Layfield LJ, Glasgow BJ. Aspiration cytology of clear-cell lesions of the parotid gland: morphologic features and differential diagnosis. Diagn Cytopathol. 1993;9(6):705–11.
20. Rossi ED, Field AS, Ali SZ, Chandra A, Gong Y, Maleki Z, et al. Suspicious for Malignancy. The Milan system for reporting Salivary Gland cytopathology. Switzerland: Springer; 2018. pp. 85-96.
21. Mehrotra S, Al-Abbadi MA, Barkan GA, Pambuccian SE, Vielh P, Wang H, et al. Malignant. The Milan system for reporting Salivary Gland cytopathology. Switzerland: Springer; 2018. pp. 97-139.
22. Vander PV, Triantafyllou A, Thompson LD, Bishop J, Hauben E, Hunt J, et al. Salivary acinic cell carcinoma: reappraisal and update. Eur Arch Otorhinolaryngol. 2016;273(11):3511–31.
23. Bishop JA, Yonescu R, Batista DA, Westra WH, Ali SZ. Cytopathologic features of mammary analogue secretory carcinoma. Cancer Cytopathol. 2013;121(5):228–33.
24. Seethala RR, Barnes EL, Hunt JL. Epithelial-myoepithelial carcinoma: a review of the clinicopathologic spectrum and immunophenotypic characteristics in 61 tumors of the salivary glands and upper aerodigestive tract. Am J Surg Pathol. 2007;31(1):44–57.
25. Williams L, Thompson LD, Seethala RR, Weinreb I, Assaad AM, Tuluc M, et al. Salivary duct carcinoma: the predominance of apocrine morphology, prevalence of histologic variants, and androgen receptor expression. Am J Surg Pathol. 2015;39(5):705–13.
26. Coca-Pelaz A, Rodrigo JP, Triantafyllou A, Hunt JL, Rinaldo A, Strojan P, et al. Salivary mucoepidermoid carcinoma revisited. Eur Arch Otorhinolaryngol. 2015;272(4):799–819.
27. Coca-Pelaz A, Rodrigo JP, Bradley PJ, Vander Poorten V, Triantafyllou A, Hunt JL, et al. Adenoid cystic carcinoma of the head and neck—an update. Oral Oncol. 2015;51(7):652–61.

28. Savera AT, Sloman A, Huvos AG, Klimstra DS. Myoepithelial carcinoma of the salivary glands: a clinicopathologic study of 25 patients. Am J Surg Pathol. 2000;24(6):761–74.
29. Petersson F. High-grade transformation (“dedifferentiation”) -malignant progression of salivary gland neoplasms, including carcinoma ex pleomorphic adenoma: a review. AJSP: Reviews & Reports. 2015;20(1):27–37.
30. Pantanowitz L, Thompson LD, Rossi ED. Diagnostic approach to fine needle aspirations of cystic lesions of the salivary gland. Head and neck pathology. 2018;12(4):548-61.
31. Jain R, Gupta R, Kudesia M, Singh S. Fine needle aspiration cytology in diagnosis of salivary gland lesions: A study with histologic comparison. Cytojournal. 2013;10:5.
32. Thiryayi SA, Low YX, Shelton D, Narine N, Slater D, Rana DN. A retrospective 3-year study of salivary gland FNAC with categorisation using the Milan reporting system. Cytopathology. 2018;29(4):343-8.
33. Rohilla M, Singh P, Rajwanshi A, Gupta N, Srinivasan R, Dey P, et al. Three-year cytohistological correlation of salivary gland FNA cytology at a tertiary center with the application of the Milan system for risk stratification. Cancer Cytopathol. 2017;125(10):767-75.
34. Tommola E, Tommola S, Porre S, Kholová I. Salivary gland FNA diagnostics in a real-life setting: one-year-experiences of the implementation of the Milan system in a tertiary care center. Cancers. 2019;11(10):1589.
35. Kala C, Kala S, Khan L. Milan system for reporting salivary gland cytopathology: An experience with the implication for risk of malignancy. Journal of cytology. 2019;36(3):160-4.
36. Savant D, Jin C, Chau K, Hagan T, Chowdhury M, Koppenhafer J, et al. Risk stratification of salivary gland cytology utilizing the Milan system of classification. Diagnostic cytopathology. 2019;47(3):172-80.

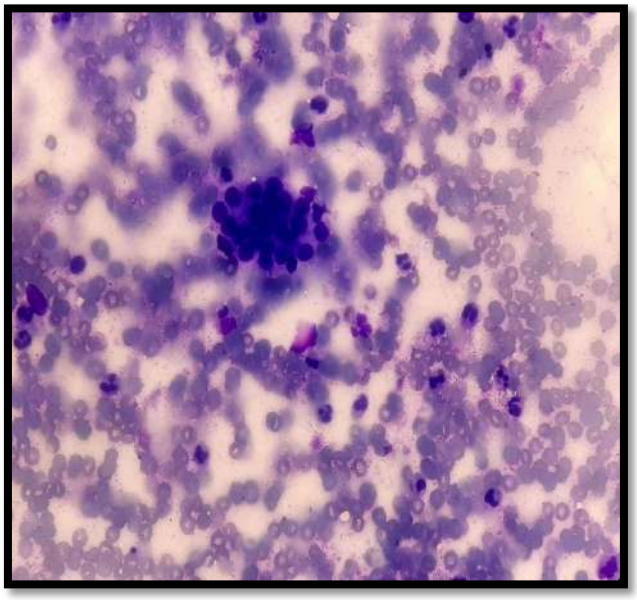
37. Wu HH, Alruwaii F, Zeng BR, Cramer HM, Lai CR, Hang JF. Application of the Milan system for reporting salivary gland cytopathology: a retrospective 12-year bi-institutional study. American journal of clinical pathology. 2019;151(6):613-21.
38. Lee JJ, Tan HM, Chua DY, Chung JG, Nga ME. The Milan system for reporting salivary gland cytology: A retrospective analysis of 1384 cases in a tertiary Southeast Asian institution. Cancer Cytopathology. 2020;128(5):348-58.
39. Amita K, Rakshitha HB, Singh A, Shankar SV. Evaluation of accuracy of Milan system for reporting salivary gland cytology: review of morphology and diagnostic challenges in each category. Journal of Cytology. 2020;37(1):18-25.
40. Dubucs C, Basset C, D'Aure D, Courtade-Saïdi M, Evrard SM. A 4-Year Retrospective Analysis of Salivary Gland Cytopathology Using the Milan System for Reporting Salivary Gland Cytology and Ancillary Studies. Cancers. 2019;11(12):1912.
41. Gaikwad VP, Anupriya C, Naik LP. Milan system for reporting salivary gland cytopathology–An experience from Western Indian Population. Journal of Cytology. 2020;37(2):93-8.
42. Jalaly JB, Farahani SJ, Baloch ZW. The Milan system for reporting salivary gland cytopathology: A comprehensive review of the literature. Diagnostic Cytopathology. 2020;48(10):880-9.
43. Young A, Okuyemi OT. Malignant Salivary Gland Tumors. StatPearls [Internet]. 2020.
44. Mukundapai M, Sharma N, Patil A, Gopal C. Fine-needle aspiration cytology of salivary gland lesions: A revised classification based on "Milan system"—4years experience of tertiary care cancer center of South India. Journal of Cytology. 2020;37(1):12-7.
45. Hafez NH, Abusinna ES. Risk assessment of salivary gland cytological categories of the Milan system: a retrospective cytomorphological and

immunocytochemical institutional study. Turk Patoloji Derg. 2020;36(2):142-53.

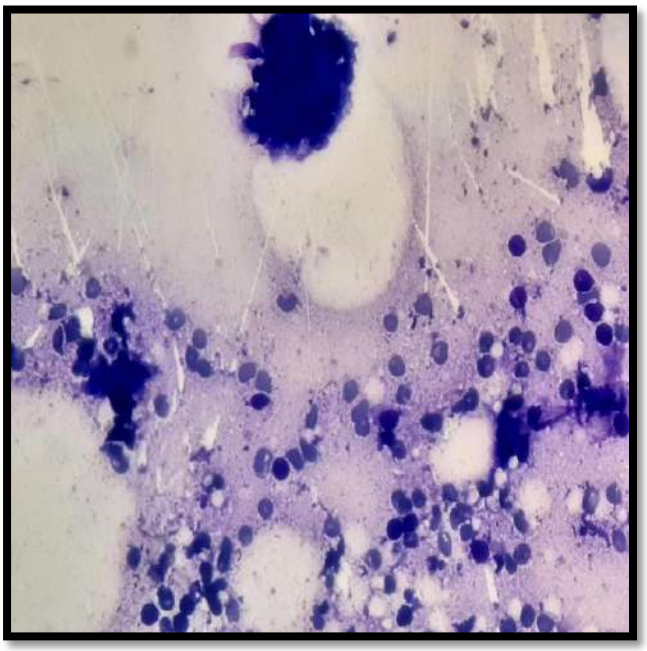
46. Das DK, Petkar MA, Al-Mane NM, Sheikh ZA, Mallik MK, Anim JT. Role of fine needle aspiration cytology in the diagnosis of swellings in the salivary gland regions: a study of 712 cases. Medical Principles and Practice. 2004;13(2):95-106.
47. Jaiswal P, Sharma M, Ahmad F, Khan NS, Shanker SS, Agarwal M. Risk-based stratification of salivary gland lesions on cytology: An institutional experience. Iranian Journal of Pathology. 2018;13(2):220-8.
48. Tyagi R, Dey P. Diagnostic problems of salivary gland tumors. Diagn Cytopathol. 2015;43(6):495–509.
49. Wangsiricharoen S, Maleki Z. Risk stratification and clinical outcome in the atypia of undetermined significance category in the Milan System for Reporting Salivary Gland Cytopathology. Cancer Cytopathology. 2020.
50. Rivera Rolon M, Schnadig VJ, Faiz S, Nawgiri R, Clement CG. Salivary gland fine-needle aspiration cytology with the application of the Milan system for risk stratification and histological correlation: A retrospective 6-year study. Diagnostic Cytopathology. 2020.
51. Maleki Z, Allison DB, Butcher M, Kawamoto S, Eisele DW, Pantanowitz L. Application of the Milan System for Reporting Salivary Gland Cytopathology to cystic salivary gland lesions. Cancer Cytopathol. 2020.
52. Faquin WC, Rossi ED. The Milan System for Reporting Salivary Gland Cytopathology. 1st ed. Switzerland: Springer; 2018.
53. Nuzhat S, Yasin SB, Nazia B, Hussain BI, Huzaifa N, Jan U, et al. Cytology of Salivary gland lesions with Histopathological correlation: A three year study in a tertiary care hospital. Research. 2019;11(03):2368-73.

54. Lee DY, Song S, Yang SK, Lee MH, Kim JE, Jung YH, et al. Prediction of Malignancy in Salivary Gland Tumors by a New Cytology Reporting System. Ear, Nose & Throat Journal. 2020:0145561320927912.
55. Dandapat MC, Rath BK, Patnaik BK, Dash SN. Tumors of salivary glands. Indian J Surg. 1991;53:200.
56. Sung S, Viswanathan K, Scognamiglio T, Yang GC, Rao R. Cytomorphology of salivary gland neoplasms: select entities and updates on the available ancillary tests and the Milan System of Reporting Salivary Gland Cytopathology. Diagnostic Histopathology. 2018;24(10):417-28.
57. Manucha V, Gonzalez MF, Akhtar I. Impact of the Milan System for Reporting Salivary Gland Cytology on risk assessment when used in routine practice in a real-time setting. Journal of the American Society of Cytopathology. 2020.
58. Hughes JH, Volk EE, Wilbur DC. Cytopathology Resource Committee CoAP. Pitfalls in salivary gland fine-needle aspiration cytology: lessons from the college of American pathologists interlaboratory comparison program in nongynecologic cytology. Arch Pathol Lab Med. 2005;129(1):26-31.
59. Griffith CC, Pai RK, Schneider F. Salivary gland tumor fineneedle aspiration cytology: a proposal for a risk stratification classification. Am J Clin Pathol. 2015;143:839-853.
60. Hang JF, Alruwaii F, Zeng BR, Lai CR, Wu HH. Subtyping salivary gland neoplasm of uncertain malignant potential based on cell type demonstrates differential risk of malignancy. Cancer Cytopathology. 2018;126(11):924-33.
61. Liu H, Ljungren C, Lin F, Zarka MA, Chen L. Analysis of histologic follow-up and risk of malignancy for salivary gland neoplasm of uncertain malignant potential proposed by the Milan System for Reporting Salivary Gland Cytopathology. Cancer cytopathology. 2018;126(7):490-7.

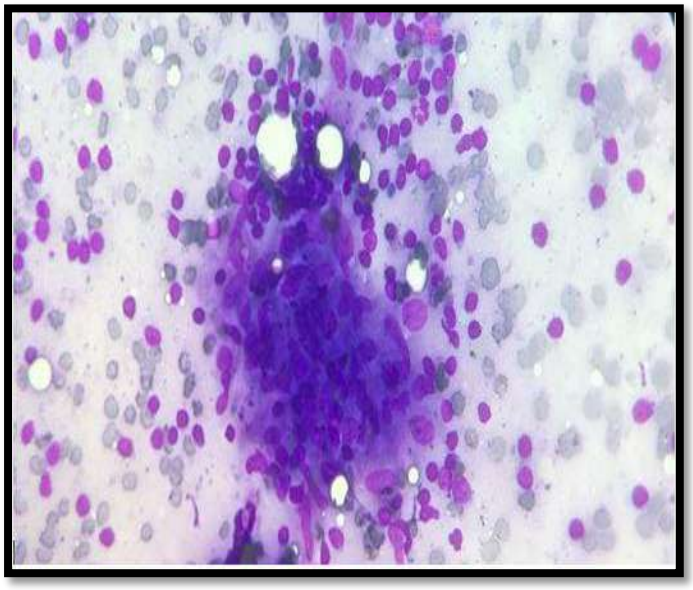
62. Young JA. Diagnostic problems in fine needle aspiration cytopathology of the salivary glands. J Clin Pathol. 1994;47:193-8.
63. Orell SR. Diagnostic difficulties in the interpretation of fine needle aspirates of salivary gland lesions: the problem revisited. Cytopathology. 1995;6:285-300.
64. Chen YA, Wu CY, Yang CS. Application of the Milan System for Reporting Salivary Gland Cytopathology: A retrospective study in a tertiary institute. Diagnostic cytopathology. 2019;47(11):1160-7.
65. Montezuma D, Canberk S, Aydın O, Dermirhas MP, Vieira AF, Goksel S, et al. A comparison study of the reporting systems for salivary gland fine needle aspirations: Are they really different?. Diagnostic Cytopathology. 2018;46(10):859-63.
66. Wei S, Layfield LJ, LiVolsi VA, Montone KT, Baloch ZW. Reporting of fine needle aspiration (FNA) specimens of salivary gland lesions: a comprehensive review. Diagnostic cytopathology. 2017;45(9):820-7.
67. Wang H, Hoda RS, Faquin W, Rossi ED, Hotchandani N, Sun T, et al. FNA biopsy of secondary nonlymphomatous malignancies in salivary glands: a multi-institutional study of 184 cases. Cancer cytopathology. 2017;125(2):91-103.
68. Salehi S, Maleki Z. Diagnostic challenges and problem cases in salivary gland cytology: a 20-year experience. Cancer cytopathology. 2018;126(2):101-11.



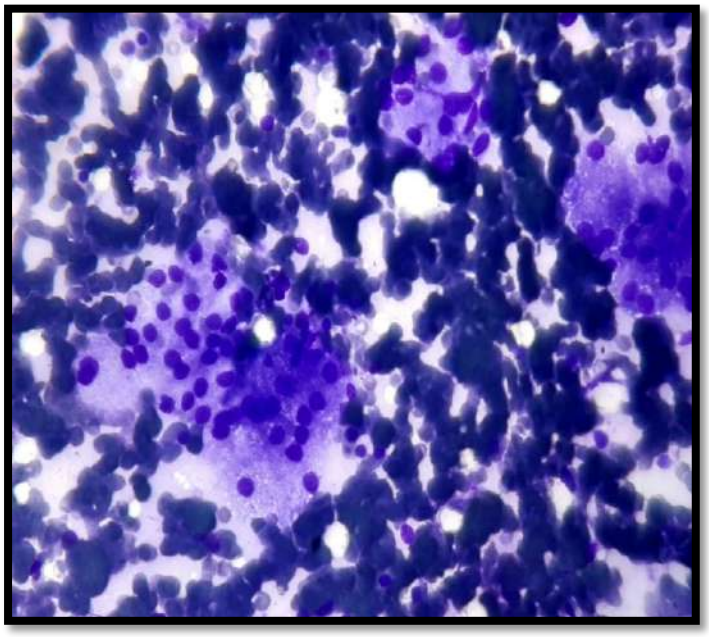
Picture 1: Category II- Non neoplastic- Acute Sialadenitis
Photomicrograph shows clusters of ductal epithelial cells against a background of neutrophils and red blood cells (Giemsa 400X)



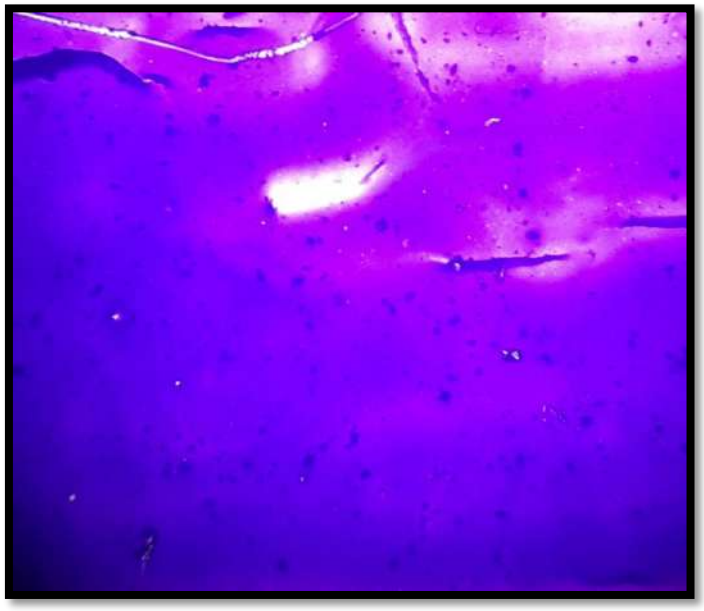
Picture 2: Category II- Non neoplastic- Chronic Sialadenitis
Photomicrograph shows clusters of salivary gland ductal epithelial cells present in a haemorrhagic background containing numerous lymphocytes. (Giemsa 400X)



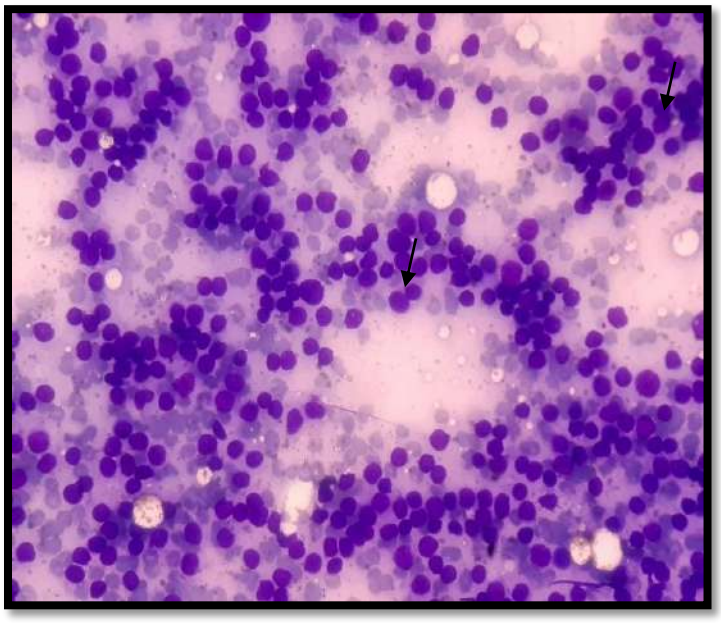
Picture 3: Category II- Non neoplastic- Granulomatous Sialadenitis
Photomicrograph shows a well formed epithelioid cell granuloma admixed with lymphocytes (Giemsa, 400X).



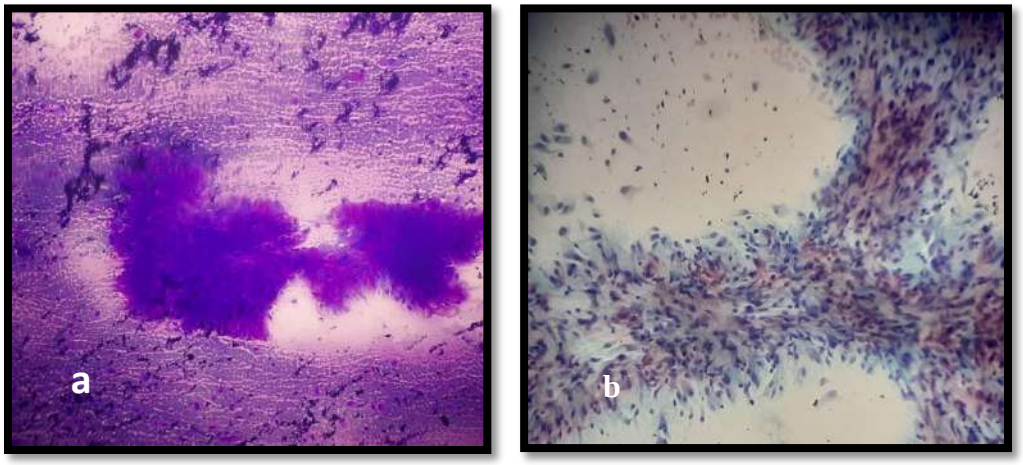
Picture 4: Category II- Non neoplastic- Sialadenosis
Photomicrograph shows clusters of enlarged salivary gland acini with stripped nuclei in the haemorrhagic background (Giemsa 400X)



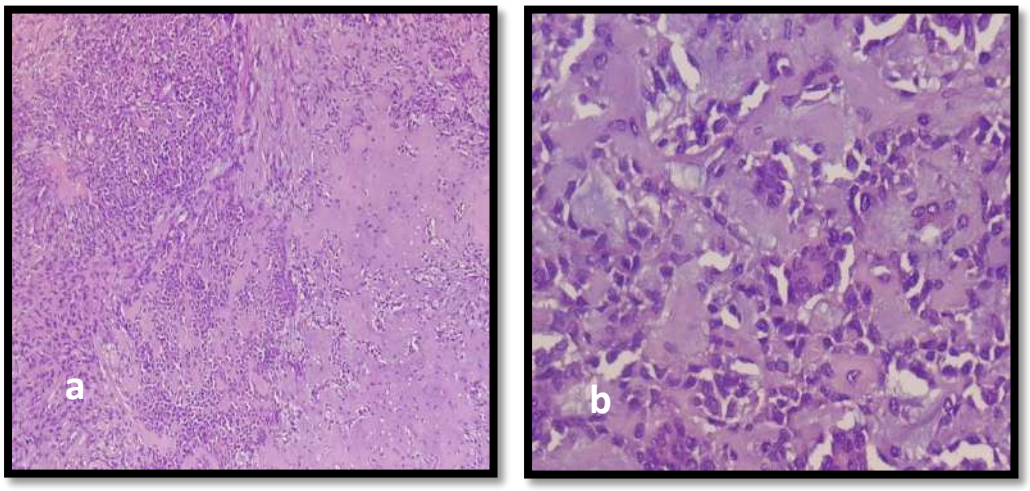
Picture 5: Category III- AUS
Photomicrograph shows scantily cellular smears with dense mucoid material (Giemsa- 400X)



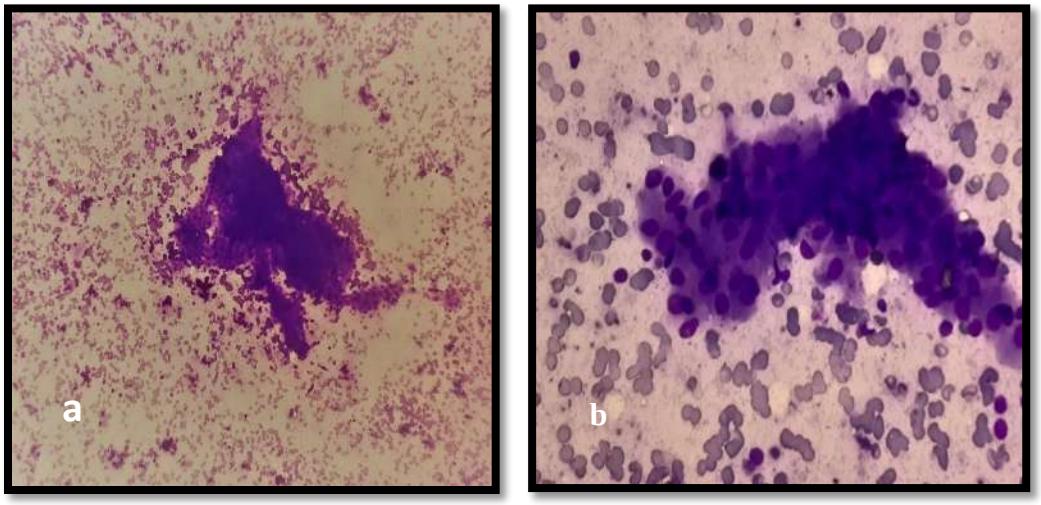
Picture 6: Category III- AUS
Photomicrograph shows reactive lymphoid cells with few large atypical cells. (arrow) (Giemsa 400X)



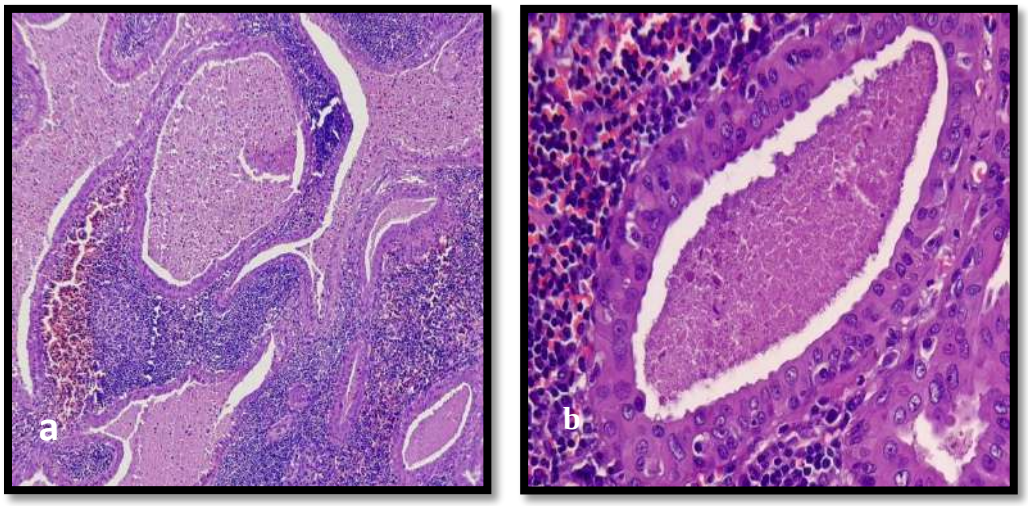
Picture 7: Category IV a- Benign- Pleomorphic Adenoma
Photomicrograph shows chondromyxoid stromal fragments within which are embedded epithelial cells and myoepithelial cells. (a &b -Giemsa 100X and PAP- 400X)



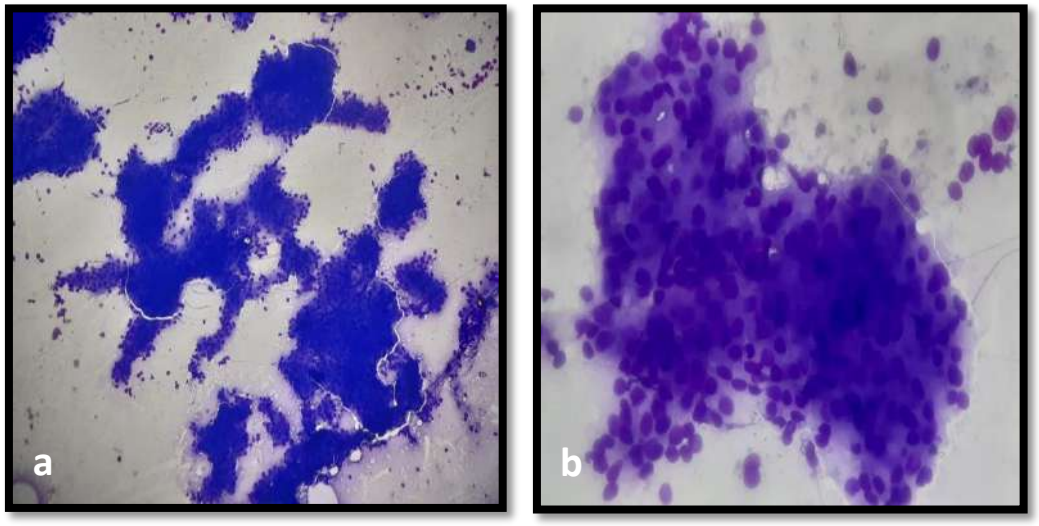
Picture 8: Photomicrograph of Pleomorphic Adenoma –:Section shows epithelial component arranged in the form of tubules and acini admixed with myoepithelial cells in a chondromyxoid stroma (a & b -H&E 100X and 400X).



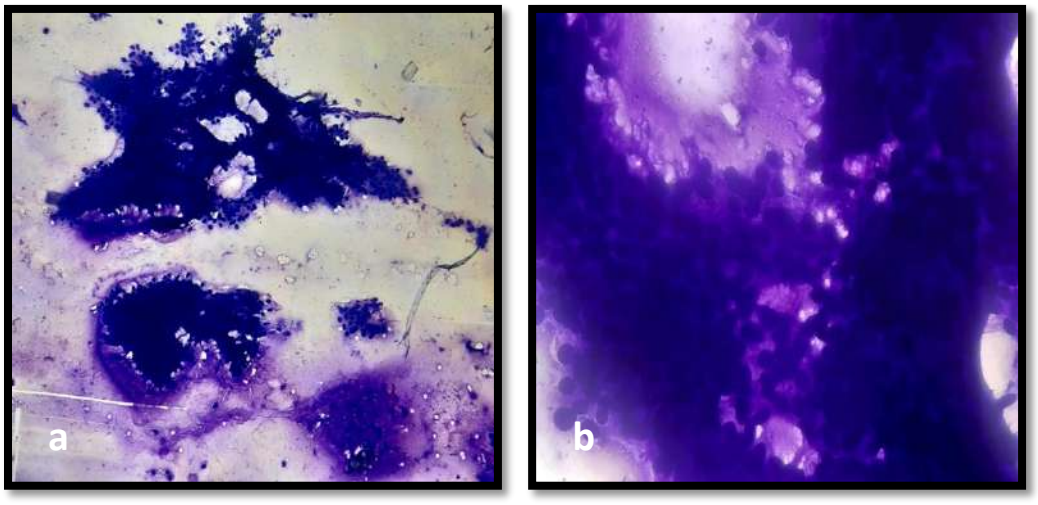
Picture 9 Category IV a- Benign- Warthins tumor
Photomicrograph shows clusters of oncocytes having abundant granular cytoplasm present against a dirty proteinacous background containing lymphocytes (a & b - Giemsa 100X, 400X)



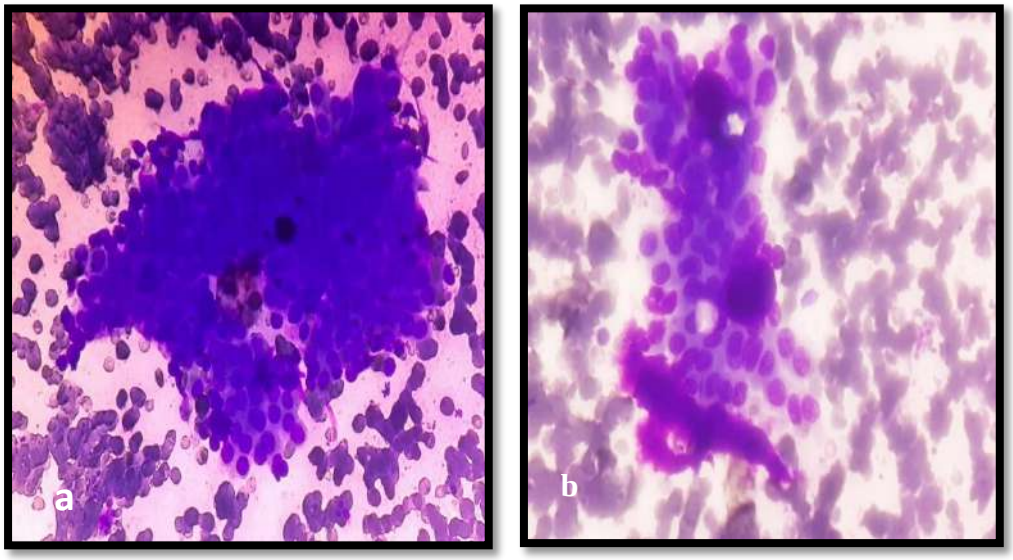
Picture 10: Photomicrograph of Warthins tumor - Sections show large cysts lined by oncocytes and separated by dense lymphoid infiltrate (a & b- H&E 100X, 400X)



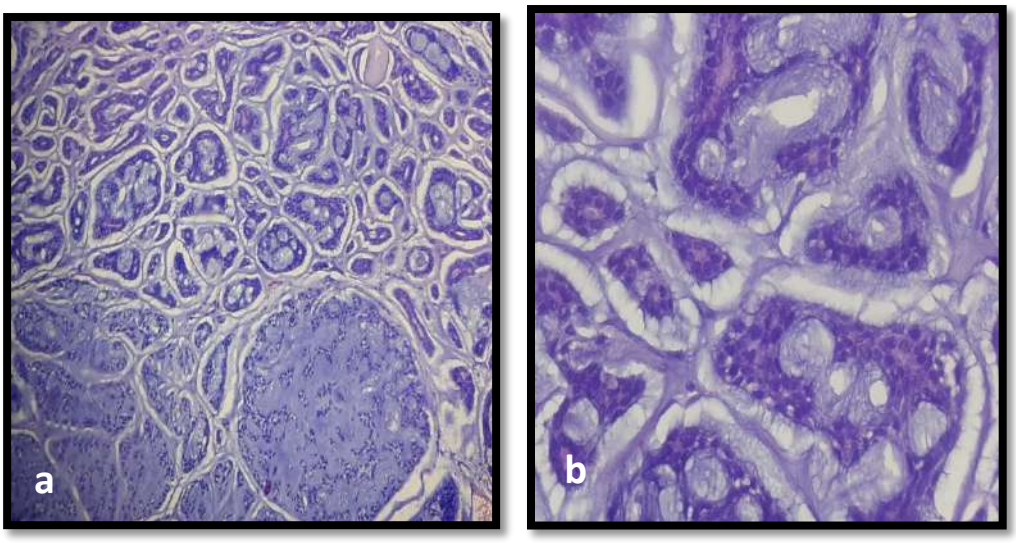
Picture 11: Category IV b- SUMP, Oncocytoid
Photomicrograph shows cellular smears with papillaroid clusters of cells having round nuclei and moderate amount of eosinophilic granular cytoplasm (a & b- Giemsa, 100X and 400X)



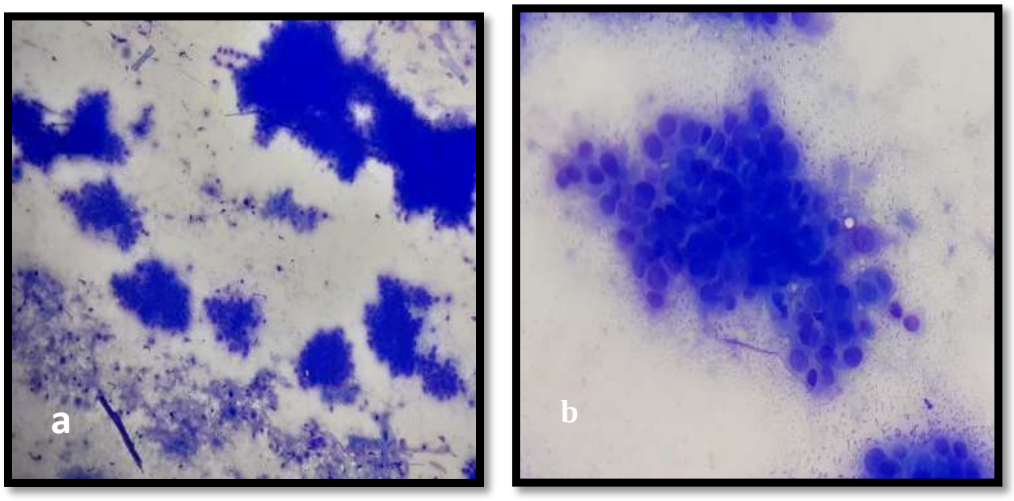
Picture 12: Category IV b- SUMP, Basaloid
Photomicrograph shows cellular smears with clusters of epithelial cells having round nuclei and scant amount of cytoplasm (a & b- Giemsa, 100X and 400X)



Picture 13: Category VI- Malignant
Photomicrograph shows cohesive and multilayered dense cell clusters (a, Giemsa 100X) Hyaline globule and extracellular hyaline material surrounded by tumor cells (b, Giemsa 400X)- Adenoid cystic carcinoma

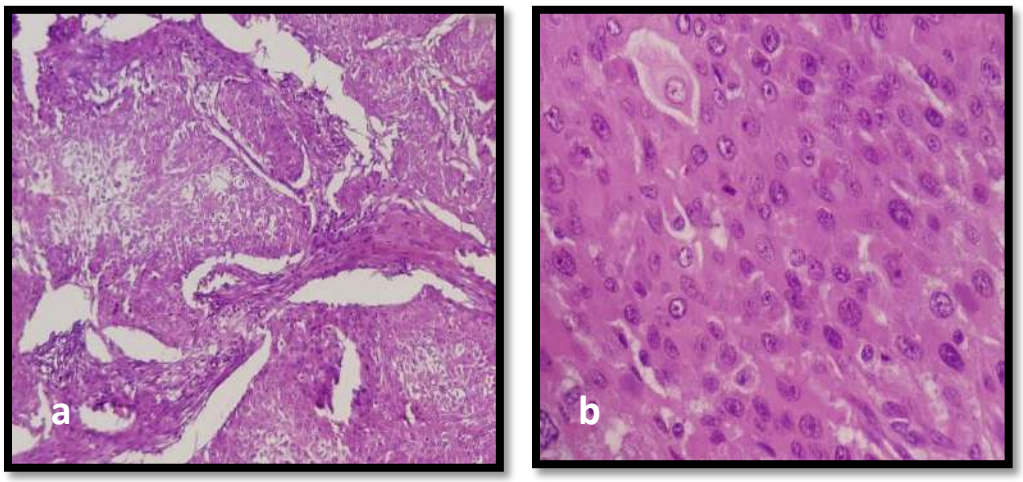


Picture 14: Photomicrograph shows tumor cells arranged in cribriform and tubular pattern (a & b- H&E- 100X and 400X)- Adenoid Cystic Carcinoma



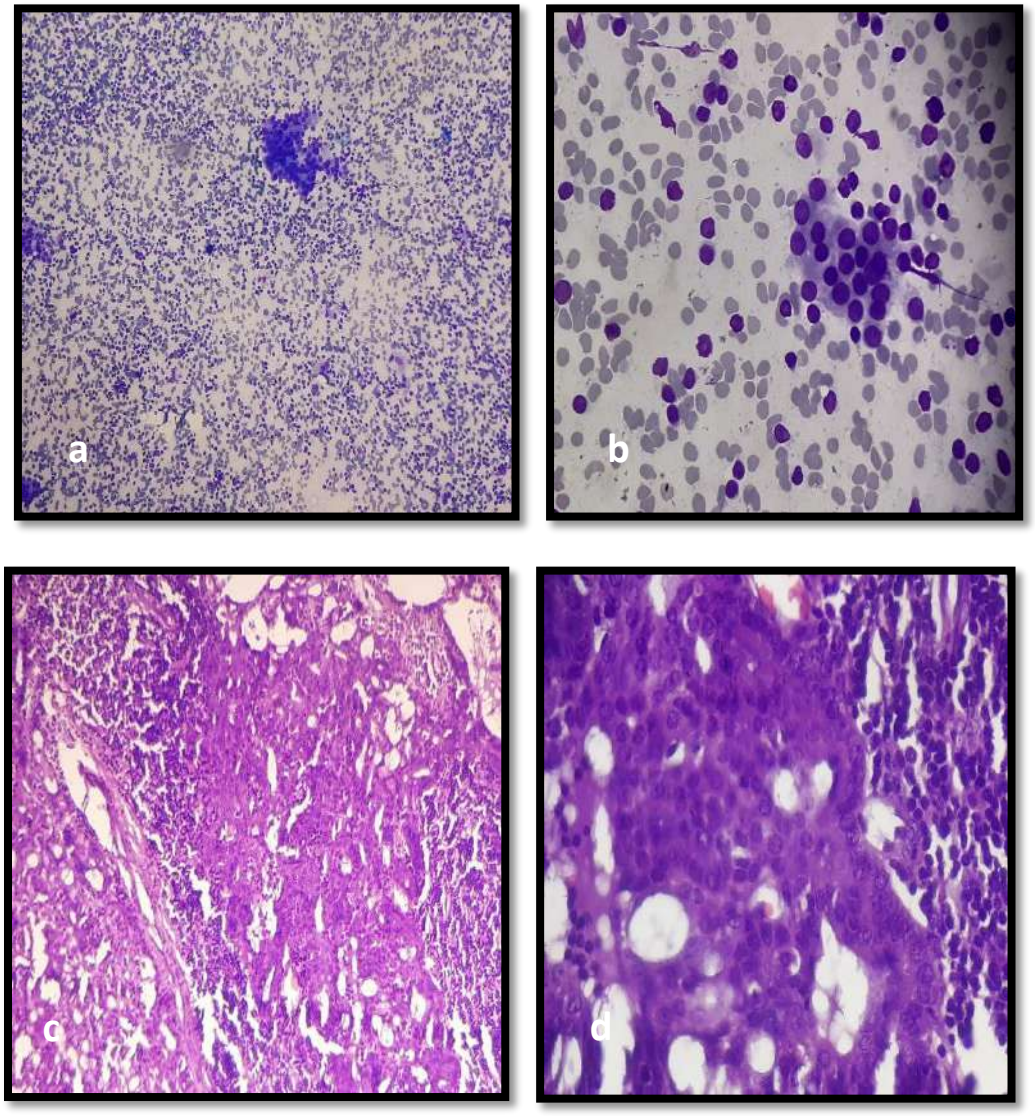
Picture 15: Category VI- Malignant

Photomicrograph shows clusters and singly scattered atypical pleomorphic cells. (a & b – Giemsa 100X and 400X) - High grade carcinoma



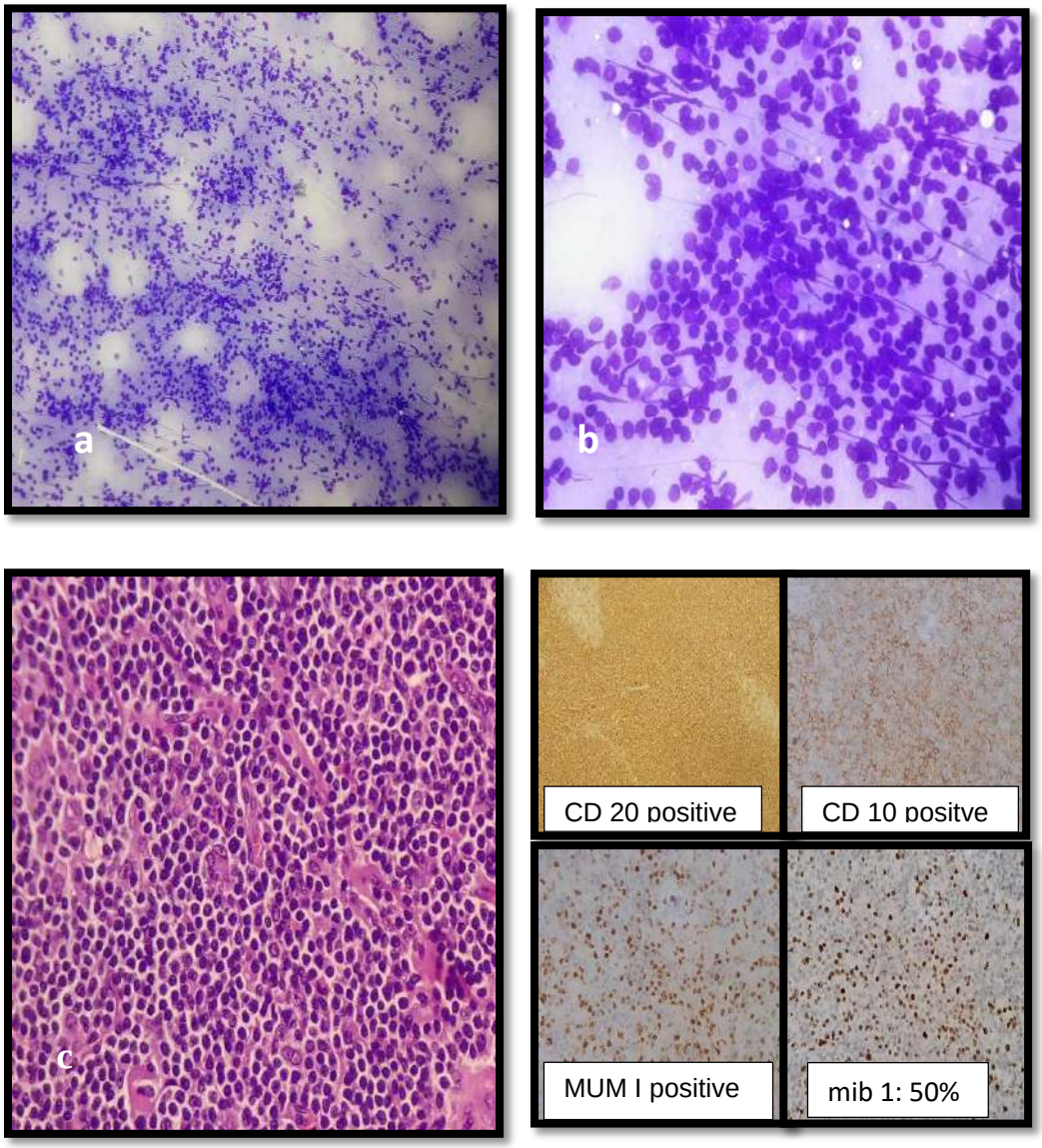
Picture 16:

Photomicrograph shows nests of large pleomorphic cells having round to oval vesicular nuclei, prominent nucleoli and abundant cytoplasm. (a & b – H&E 100X and 400X)- High grade carcinoma



Picture 17: Discordant Case- Category IV a- Warthins tumor on cytology and Metastasis of Acinic Cell Carcinoma in intraparotid lymph node on histopathology.

Photomicrograph of aspiration smears show dense lymphoid population with oncocytic cells. (a & b Giemsa, 100X & 400X) The histology of the same revealed metastasis of Acinic Cell Carcinoma in intraparotid lymph node (c&d H&E 100X&400X)



Picture 18: Discordant Case- Category II on cytology and Diffuse large B cell lymphoma(Germinal center type) on histopatholgy and IHC Photomicrograph of smears show reactive lymphoid cells with few atypical cells that were labelled as reactive immunoblasts. (a&b- Giemsa, 100X & 400X). The same was diagnosed as Diffuse large B cell lymphoma (Germinal center type) on histopathology and IHC. (c-H&E 400X)

S.No	MRD No	Asp No	INITIALS	Age	Sex	Site of lesion	Size of lesion	Change in size of lesion	uni / bilateral	Pain	Asso with eating	signs of inflammation	co morbidities	Smoking/ tobacco chewing	well ciecumscribed swelling	mobile / immobile
1	12358	15-1054	NA	51	F	rt parotid	2x1cm	increasing	uni	no	no	none	none	na	yes	immobile
2	12458	15-1068	M	38	F	lt submandibular	1.5x1.5cm	increasing	uni	no	no	none	none	na	yes	immobile
3	145632	15-1090	R	50	M	lt parotid	2x2cm	increasing	uni	no	no	none	none	yes	yes	immobile
4	127546	15-1127	MS	27	M	parotid	3x3cm	increasing	uni	no	no	none	none	na	yes	immobile
5	132938	15-1169	KK	40	F	lt parotid	1.5x1cm	increasing	uni	no	no	none	none	na	yes	immobile
6	583903	15-1195	TL	86	M	Rt submandibular	1x0.5cm	no	uni	no	dysphagia	none	none	na	yes	immobile
7	152412	15-1294	DB	80	M	lt parotid	4x2.5cm	increasing	uni	no	no	none	HTN and DM	na	yes	immobile
8	154917	15-1326	SK	50	F	rt parotid	4x4cm	no	uni	no	no	none	none	na	yes	immobile
9	687749	15-1401	SC	62	M	Rt submandibular	1x1cm	no	uni	no	no	none	none	na	yes	immobile
10	155602	15-1453	G	16	M	Lt submandibular	1x1cm	no	uni	no	no	none	none	na	yes	immobile
11	175981	15-1460	SD	70	F	rt parotid	2x2cm	increasing	uni	no	no	none	none	na	yes	immobile
12	183408	15-1497	I	53	M	Rt parotid	3x3cm	no	uni	no	no	none	none	na	yes	immobile
13	183838	15-1498	R	60	F	B/L parotid	3x3l, 1x2cmr	increasing	bilateral	no	no	none	none	na	yes	immobile
14	186503	15-1517	VK	52	M	left submandibular	1x1cm	increasing	uni	no	no	none	none	na	yes	immobile
15	182457	15-1520	L	70	F	rt submandibular	1x1cm	no	uni	no	no	none	none	na	yes	immobile
16	129294	15-1573	KS	60	M	Rt submandibular	1x1cm	no	uni	no	exxagerated after eating	none	none	na	yes	immobile
17	202260	15-1560	AS	79	M	Rt parotid	4x3cm	no	uni	no	no	none	none	na	yes	immobile
18	195412	15-1617	PK	52	F	lt parotid	1.5x1cm	increasing	uni	no	no	none	none	na	yes	immobile
19	207515	15-1672	GH	58	M	lt submandibular	1x1cm	increasing	uni	no	no	none	none	na	yes	immobile
20	849907	15-1701	SS	66	M	lt parotid	3x3cm	increasing	uni	no	no	none	none	na	yes	immobile
21	218768	15-1763	S	20	M	rt parotid	1.5x1.5cm	increasing	uni	no	exxagerated after eating	none	none	na	yes	immobile
22	207431	15-1827	N	32	M	lt parotid	0.5x0.8cm	no	uni	no	no	none	none	na	yes	immobile
23	257833	15-1987	S	29	F	rt parotid	7x6cm	no	uni	no	no	none	none	na	yes	immobile
24	259415	15-2041	P	58	F	Lt parotid	1x1cm	increasing	uni	no	no	none	none	na	yes	immobile
25	232	16--01	R	32	M	rt parotid	3x3cm	no	uni	no	no	none	none	na	yes	immobile
26	4179	16--09	JRK	63	F	rt parotid	4x3cm	no	uni	no	no	none	none	na	yes	immobile
27	159246	16-23	DG	50	M	lt parotid	3x2cm	no	uni	no	no	none	none	na	yes	immobile
28	5933	16-39	KK	40	F	Lt parotid	1x0.5cm	increasing	uni	no	no	none	none	na	yes	immobile
29	19611	16-125	C	50	M	rt parotid	2.5x1cm	no	uni	no	no	none	none	na	yes	immobile
30	36413	16-230	M	34	M	Rt submandibular	2.5x1.5cm	no	uni	no	exxagerated after eating	none	none	na	yes	immobile
31	44520	16-294	P	30	M	Rt submandibular	2x1cm	increasing	uni	no	no	none	none	na	yes	immobile
32	44861	16-298	R	24	F	rt parotid	2x1cm	no	uni	no	no	none	none	na	yes	immobile
33	49653	16-339	H	18	F	lt palate	3x2cm	no	uni	no	no	none	none	na	yes	immobile
34	54893	16-361	JS	45	M	Rt submandibular	2x3cm	increasing	uni	no	no	none	none	na	yes	immobile
35	22222	16-375	JR	62	M	rt parotid	2x2cm	increasing	uni	present	no	tender	DM 2	na	yes	immobile
36	76200	16-498	JK	70	F	rt parotid	0.5x0.5cm	no	uni	no	no	none	k/c/o Ca Breast	na	yes	immobile
37	81127	16-534	GS	50	M	palate	1x1cm	no	uni	no	no	none	none	na	yes	immobile
38	81256	16-547	N	38	M	Rt submandibular	1x1cm	no	uni	no	exxagerated after eating	none	none	na	yes	immobile
39	102861	16-686	GS	44	M	rt parotid	3x2.5cm	no	uni	no	no	none	none	na	yes	immobile
40	29192	16-745	SBS	64	M	rt parotid	3x2.5cm	increasing	uni	present	no	none	none	na	yes	immobile
41	109266	16-759	JS	72	F	Rt submandibular	1x1cm	no	uni	no	no	none	none	na	yes	immobile
42	111549	16-794	KK	60	F	rt parotid	4x2.5cm	increasing	uni	no	no	none	none	na	yes	immobile
43	56983	16-919	GK	65	F	rt parotid	4x4cm	no	uni	no	no	tender	none	na	yes	immobile
44	65478	16-984	SR	70	F	lt parotid	1.5x1.5cm	no	uni	no	no	none	HTN	na	yes	immobile
45	90625	16-1186	SK	11	F	lt parotid	1x1cm	no	uni	present	no	none	k/c/o low grade mucoepidermoid carcinoma	na	yes	immobile
46	139244	16-1288	JS	55	M	lt parotid	1.5x1.5cm	increasing	uni	no	no	none	k/c/o sq cell ca maxilla	yes	yes	immobile
47	111317	16-1374	Y	55	M	rt parotid	3.5x2cm	increasing	uni	no	no	none	HTN and DM	na	yes	immobile
48	119819	16-1454	GK	46	F	rt parotid	3x3cm	increasing	uni	no	no	none	none	na	diffuse	immobile
49	157311	16-1582	PK	44	F	Rt submandibular	2x1.5cm	increasing	uni	no	no	none	none	na	yes	immobile
50	141150	16-1615	AK	24	F	rt parotid	2.5x2cm	increasing	uni	no	no	none	none	na	yes	immobile
51	934	17-68	SC	50	M	rt parotid	1x1cm	no	uni	no	no	none	HTN	m	yes	immobile
52	185068	17-88	PS	63	F	rt parotid	4x3cm	no	uni	no	no	none	none	na	yes	immobile
53	186199	17-92	B'	48	F	rt parotid	3x2cm	no	uni	no	no	none	none	na	yes	immobile
54	194652	17-156	NK	40	F	rt parotid	1x1cm	no	uni	no	no	none	none	na	yes	immobile
55	242435	17-536	RK	59	M	rt parotid	3x2cm	increasing	uni	no	no	none	none	na	yes	immobile
56	226261	17-557	GS	35	M	B/l parotid	2x1cmB/l	increasing	bilateral	no	no	none	DM 2	na	yes	immobile
57	251396	17-615	VK	57	M	lt parotid	3x2cm	no	uni	no	no	none	DM 2	na	yes	immobile
58	254043	17-648	S	36	M	Rt parotid	3x2cm	increasing	uni	present	no	none	none	na	yes	immobile
59	254328	17-652	VS	62	M	lt parotid	1x1cm	increasing	uni	no	no	none	HTN and DM	na	yes	immobile
60	265916	17-732	JS	58	M	B/L parotid	b/l 2cm	increasing	bilateral	no	no	none	none	na	yes	immobile
61	172408	17-871	JS	52	M	rt parotid	4x2cm	increasing	uni	no	no	none	HTN	na	yes	immobile
62	283623	17-891	JK	37	F	rt parotid	2x1cm	increasing	uni	no	no	none	none	na	yes	immobile
63	81352	17-943	KG	57	F	lt parotid	4x3cm	increasing	uni	no	no	none	k/c/o sjogren syndrome	na	yes	immobile
64	293757	17-1006	S	47	M	rt parotid	3x2cm	increasing	uni	no	no	none	none	yes	yes	immobile
65	302645	17-1070	SR	70	M	lt parotid	3x3cm	increasing	uni	no	no	none	none	na	yes	immobile
66	303248	17-1098	KM	74	M	Lt submandibular	3x3cm	increasing	uni	no	no	none	DM 2	na	yes	immobile
67	308486	17-1123	ML	84	M	rt parotid	2x2cm	increasing	uni	no	no	none	none	na	yes	immobile
68	310889	17-1146	PP	52	M	Rt submandibular	1x1cm	increasing	uni	no	no	none	none	na	yes	immobile

S.No	MRD No	Asp No	Radiology	radiology solid /cystic/ complex	Site of FNAC	FNA diag	classification under MSRSGC	Histopathology correlation	Mode of procedure
1	12358	15-1054	na	na	rt parotid	pleomorphic adenoma	IV benign	-	Direct
2	12458	15-1068	na	na	lt submandibular	cystic lesion	II	-	Direct
3	145632	15-1090	na	na	lt parotid	chronic sialadenitis	II	-	Direct
4	127546	15-1127	na	na	left angle of jaw	pleomorphic adenoma	IV benign	-	Direct
5	132938	15-1169	na	na	left infraauricular	pleomorphic adenoma	IV benign	-	Direct
6	583903	15-1195	na	na	rt submandibular	sialadenitis	II	-	Direct
7	152412	15-1294	homogenously enhancing lesion in left parotid	solid	left parotid	pleomorphic adenoma	IV benign	-	Direct
8	154917	15-1326	na	na	rt parotid	pleomorphic adenoma	IV benign	-	Direct
9	687749	15-1401	na	na	rt submandibular	non neoplastic	II	-	Direct
10	155602	15-1453	na	na	lt submandibular	nondiagnostic	I	-	Direct
11	175981	15-1460	na	na	rt preauricular	pleomorphic adenoma	IV benign	-	Direct
12	183408	15-1497	b/l parotid are enlarged	solid	rt parotid	sialadenosis	II	-	Direct
13	183838	15-1498	pleomorphic adenoma- b/l parotids	solid	b/l parotids	Warthins tumor	IV benign	-	Direct
14	186503	15-1517	submandibular sialdenitias	solid	lt submandibular	chronic sialadenitis	II	Chronic sialadenitis	Direct
15	182457	15-1520	na	na	Rt submndibular gland	malignant	VI	occasional stromal fragmets - cell block	Direct
16	129294	15-1573	na	na	rt submandibular	acute on chronic sialadenitis	II	-	Direct
17	202260	15-1560	na	na	rt parotid	pleomorphic adenoma	IV benign	-	Direct
18	195412	15-1617	na	na	lt parotid	sialadenosis	II	-	Direct
19	207515	15-1672	na	na	lt submandibular	pleomorphic adenoma	IV benign	-	Direct
20	849907	15-1701	na	na	lt parotid	benign cystic lesion. II	II	-	Direct
21	218768	15-1763	na	na	rt parotid	chronic sialadenitis	II	-	Direct
22	207431	15-1827	na	na	lt preauricular	reactive hyperplasia	II	-	Direct
23	257833	15-1987	na	na	rt preauricular	pleomorphic adenoma	IV benign	-	Direct
24	259415	15-2041	na	na	lt parotid	nondiagnostic	I	-	USG guided
25	232	16--01	na	na	Rt angle of jaw	Warthins tumor	IV Benign	-	Direct
26	4179	16--09	na	na	rt preauricular	pleomorphic adenoma	IV benign	-	Direct
27	159246	16-23	na	na	lt infrauricular	warthins tymor	IV benign	-	Direct
28	5933	16-39	na	na	lt parotid	pleomorphic adenoma	IV benign	-	Direct
29	19611	16-125	complex adenoma- rt parotid	complex	rt parotid	warthins tymor	IV benign	-	Direct
30	36413	16-230	na	na	rt submandibular	chronic sialadenitis	II	-	Direct
31	44520	16-294	na	na	lt submandibular	Acute sialadenitis	II	-	Direct
32	44861	16-298	na	na	Rt infrauricular	Acute sialadenitis	II	-	Direct
33	49653	16-339	? Minor salivary gland tumor	solid	lt patate	Pleomorphic adenoma	IV benign	-	Direct
34	54893	16-361	na	na	rt submandibular	chronic sialadenitis	II	-	Direct
35	22222	16-375	na	na	rt parotid	chronic sialadenitis	II	-	Direct
36	76200	16-498	na	na	rt post auricular	warthins tumor	IV benign	-	Direct
37	81127	16-534	na	na	palate	Pleomorphic adenoma	IV Benign	Pleomorphic adenoma	Direct
38	81256	16-547	na	na	rt submandibular	Chronic sialadenitis	II	-	Direct
39	102861	16-686	na	na	rt parotid	pleomorphic adenoma	IV benign	-	Direct
40	29192	16-745	na	na	rt preauricular	warthins tumor	IV benign	-	Direct
41	109266	16-759	na	na	rt submandibular	chr sialadenitis	II	-	Direct
42	111549	16-794	na	na	rt preauricular	cystic lesion	II	-	Direct
43	56983	16-919	na	na	rt angle of jaw	acute sialadenitis	II	-	Direct
44	65478	16-984	na	na	parotid swelling	benign cystic lesion	II	-	Direct
45	90625	16-1186	heterogenously enhancing lesion in left parotid	solid	lt parotid	malignant muco epidermoif carcinoma	VI	mucoepidermoid carcinoma	Direct
46	139244	16-1288	na	na	lt parotid	benign cyctic lesion	II	poorly differentiated malignancy- maxilla/ pterygoid place- haematopoietic elements.	Direct
47	111317	16-1374	na	na	rt parotid	sialadenosis	II	-	Direct
48	119819	16-1454	na	na	rt parotid	SUMP cystic lesion	IV SUMP	-	Direct
49	157311	16-1582	na	na	rt submandibular	cystic lesion	III	-	Direct
50	141150	16-1615	hypoechoic lesion in rt parotid	solid	rt parotid	warthins tumor	IV benign	mucoepidermoid carcinoma	Direct
51	934	17-68	complex mass with cystic component in rt parotid	complex	rt parotid	mucinous cyctic lesion	III	-	Direct
52	185068	17-88	na	na	rt infrauricular	benign cycstic lesion	II	-	Direct
53	186199	17-92	na	na	rt infrauricular	pleomorphic adenoma	IV benign	-	Direct
54	194652	17-156	na	na	rt parotid	Pleomorphic adenoma	IV benign	-	Direct
55	242435	17-536	na	na	rt parotid	SUMP	IV SUMP	-	Direct
56	226261	17-557	na	na	B/l parotid	Granulomatous sialadenitis	II	-	Direct
57	251396	17-615	na	na	lt parotid	warthins tumor	IV benign	-	Direct
58	254043	17-648	na	na	rt parotid	Acute sialadenitis	II	-	Direct
59	254328	17-652	mild homogenous contrast in left parotid	solid	lt parotid	warthins tumor	IV benign	-	Direct
60	265916	17-732	na	na	B/l parotid	warthins tumor	IV benign	-	Direct
61	172408	17-871	b/l heterogenously enhancing solid lesion in parotids	solid	rt parotid	pleomorphic adenoma	IV beingn	-	Direct
62	283623	17-891	dull hypoechoic lesion in rt parotid	solid	rt parotid	SUMP	IV SUMP	-	Direct
63	81352	17-943	na	na	lt parotid	Acute on chronic sialadenitis	II	-	Direct
64	293757	17-1006	na	na	rt parotid	Warthins tumor	IV benign	-	Direct
65	302645	17-1070	na	na	lt preauricular	pleomorphic adenoma	IV benign	-	Direct
66	303248	17-1098	?Submadibular abscess	solid	lt submandibular	chr sialadenitis	II	-	USG guided
67	308486	17-1123	? Pleomorphic adenoma	solid	rt parotid	Warthins tumor	IV benign	-	Direct
68	310889	17-1146	na	na	rt submandibular	Acute on chronic sialadenitis	II	-	Direct

S.No	MRD No	Asp No	INITIALS	Age	Sex	Site of lesion	Size of lesion	Change in size of lesion	uni / bilateral	Pain	Asso with eating	signs of inflammation	co morbidities	Smoking/ tobacco chewing	well ciecumscribed swelling	mobile / immobile
69	329561	17- 1293	PK	52	F	Lt Parotid	1x1cm	increasing	uni	no	no	none	none	na	yes	immobile
70	12568	17-1310	ND	60	F	Rt parotid	3x2cm	increasing	uni	no	no	none	none	na	yes	immobile
71	334522	17-1331	NK	48	F	Rt submandibular	2x2cm	no	uni	no	no	none	none	na	yes	immobile
72	315836	17-1451	NS	75	M	rt parotid	1x0.5cm	no	uni	no	no	none	k/c/o of Ca breast	na	yes	immobile
73	415326	18-14	RL	63	M	rt parotid	4x2cm	increasing	uni	no	no	none	none	na	yes	immobile
74	417353	18-94	NS	30	F	Lt submandibular	1.5x1cm	increasing	uni	no	no	none	none	na	yes	immobile
75	429835	18-132	LS	21	M	rt parotid	2x2cm	increasing	uni	no	no	none	none	na	yes	immobile
76	434407	18-161	JKJ	58	M	Lt submandibular	1x1cm	no	uni	no	no	none	none	na	yes	immobile
77	446821	18-263	JK	50	F	rt parotid	1x1cm	no	uni	no	no	none	none	na	yes	immobile
78	451412	18-297	JS	55	M	rt parotid	2x1cm	no	uni	no	no	none	none	na	yes	immobile
79	458780	18-384	ML	52	M	lt submandibular	1.5x1.5cm	no	uni	no	no	none	none	na	yes	immobile
80	396413	18-393	PK	42	F	rt parotid	1x1cm	no	uni	no	no	none	none	na	yes	immobile
81	472164	18-510	PS	48	M	lt parotid	3x2cm	no	uni	no	no	none	none	na	yes	immobile
82	162630	18-580	MS	12	M	rt parotid	3x2cm	no	uni	no	no	none	none	na	yes	immobile
83	484888	18-649	GS	37	M	rt parotid	2x2cm	no	uni	no	no	none	none	na	yes	immobile
84	485727	18-659	M	66	F	lt parotid	3x3cm	no	uni	no	no	none	none	na	yes	immobile
85	494283	18-749	MK	29	F	lt parotid	1x1cm	no	uni	no	no	none	none	na	yes	immobile
86	499475	18-792	GS	75	M	rt parotid	2x1cm	no	uni	no	no	none	none	na	yes	immobile
87	505427	18-865	LS	67	M	Rt submandibular	1x1cm	increasing	uni	no	no	none	none	na	yes	immobile
88	508534	18-885	NS	55	M	lt parotid	1x1cm	no	uni	no	no	none	none	yes	yes	immobile
89	515645	18-955	BS	52	M	B/L parotid	1.5x1r, 2x2cm l	no	bilateral	no	no	none	none	na	yes	immobile
90	520325	18-991	AD	37	M	soft palate	2x2cm	increasing	uni	no	no	none	none	na	yes	immobile
91	531446	18-1017	JS	45	M	Rt submandibular	2x1.5cm	increasing	uni	no	no	none	none	na	yes	immobile
92	527329	18-1045	P	30	F	rt parotid	4x4cm	increasing	uni	no	no	none	none	na	yes	immobile
93	527488	18-1049	AS	43	F	rt parotid	1.5c1.5cm	increasing	uni	no	no	none	none	yes	yes	immobile
94	65478	18-1112	SR	72	F	lt parotid	3x2cm	increasing	uni	no	no	none	none	na	yes	immobile
95	539090	18-1172	R	49	F	rt parotid	1x1cm	increasing	uni	no	no	none	none	na	yes	immobile
96	544141	18-1215	GK	15	F	Lt submandibular	1x1cm	no	uni	no	no	none	none	na	yes	immobile
97	457403	18-1406	RD	67	F	lt parotid	2x1cm	no	uni	no	no	none	k/c/o pleomorphic adenoma	na	yes	immobile
98	568810	18-1448	JS	61	F	Rt submandibular	2x1cm	no	uni	no	no	none	none	na	yes	immobile
99	554313	18-1485	S	48	F	rt parotid	1.5x1.5cm	no	uni	no	no	none	none	na	yes	immobile
100	572331	18-1535	S	75	F	Lt submandibular	1x1cm	no	uni	no	no	none	none	na	yes	immobile
101	583250	18-1580	NG	53	F	lt parotid	3x3cm	increasing	uni	no	no	none	none	yes	yes	immobile
102	595388	18-1702	HK	44	F	lt cheek	2x1.5cm	no	uni	no	no	none	none	na	yes	immobile
103	390231	18-1716	AK	70	F	rt parotid	6x4cm	increasing	uni	no	no	none	none	na	yes	immobile
104	596201	18-1718	UR	38	F	rt parotid	2x2cm	increasing	uni	no	no	none	none	na	yes	immobile
105	606515	18-1795	KK	60	F	lt parotid	1.5x1.5cm	no	uni	no	no	none	none	na	yes	immobile
106	660712	19-110	K	54	F	Left parotid	4x4cm	no	uni	no	no	none	none	na	yes	immobile
107	660742	19-143	S	72	F	Left parotid	3X2cm	increasing	uni	no	no	none	none	na	yes	immobile
108	665396	19- 156	A	20	F	Right Submandibular	2x1cm	no	uni	no	no	none	none	na	yes	immobile
109	667124	19-162	R	43	M	Left parotid	2x1cm	no	uni	no	no	none	none	na	yes	immobile
110	666849	19- 165	K	61	M	Right Submandibular	3x1.5	no	uni	no	no	none	none	na	yes	immobile
111	671386	19-190	JS	23	M	left parotid	3x2cm	increasing	uni	no	no	none	none	na	yes	immobile
112	673397	19-205	H	22	F	Right Submandibular	1.5x1cm	no	uni	no	no	none	none	na	diffuse	mobile
113	675673	19- 226	S	16	F	Left parotid	2x1cm	no	uni	no	no	none	none	na	yes	immobile
114	675498	19-222	G	69	F	right parotid	2x1cm	no	uni	no	no	none	HTN	na	yes	immobile
115	676179	19-237	P	88	F	parotid	4x3cm	increasing	uni	no	no	none	none	na	yes	immobile
116	678529	19- 248	RD	40	M	right Submandibular	1x1cm	no	uni	no	no	none	TB	yes	yes	mobile
117	669112	19-278	S	64	M	parotid	2x2cm	no	uni	no	no	none	none	na	yes	immobile
118	720630	19-624	MK	53	F	lt parotid	3x2cm	no	uni	no	no	none	none	na	yes	immobile
119	723768	19-673	HJ	54	M	left Parotid	2x2cm	increasing	uni	no	no	none	TB	na	yes	immobile
120	729515	19-733	PS	63	M	LT submandibular	3x2cm	no	uni	no	no	none	none	na	yes	immobile
121	437879	19-739	BB	65	M	Rt parotid	4x3cm	no	uni	no	no	none	none	na	diffuse	mobile
122	736763	19-804	A	60	M	Lt parotid	1.5x1.5cm	increasing	uni	no	no	none	none	na	yes	immobile
123	727780	19-806	GS	49	M	Lt parotid	4x3cm	increasing	uni	no	no	none	none	na	yes	immobile
124	529831	19-847	NB	36	M	lt submantal and lt parotid	1x1cm, 1x1.5cm	no	uni	no	no	none	none	yes	yes	immobile
125	391757	19-915	DN	45	M	Lt submandibular	1x1cm	no	uni	present	no	none	none	yes	yes	immobile
126	747950	19-930	R	25	F	Rt parotid	1x1.5cm	increasing	uni	no	no	none	none	na	yes	immobile
127	748190	19-947	KC	75	M	Rt parotid	4X4mm	no	uni	no	no	none	none	na	yes	immobile
128	750229	19-957	GS	40	M	lt parotid	1x1cm	increasing	uni	no	no	none	none	na	yes	immobile
129	727580	19-1022	AK	33	M	LT submandibular	0.5x0.5cm	no	uni	no	no	none	none	na	yes	immobile
130	781104	19-1250	KK	40	F	parotid	2x1cm	no	uni	no	no	none	none	na	diffuse	mobile
131	5020	19-1322	KP	52	M	rt parotid	1x1cm	increasing	uni	no	no	none	COPD on budesonide	yes	yes	immobile
132	784256	19-1326	RK	44	F	Lt parotid	2x1cm	no	uni	no	exxagerated after eating	none	none	na	yes	immobile
133	792798	19-1390	JS	13	M	lt parotid	3x2cm	increasing	uni	no	no	none	none	na	yes	immobile
134	795621	19-1398	UR	54	F	rt submandibular	1.5x1cm	no	uni	no	no	none	HTN	na	yes	mobile
135	332291	19- 1403	RK	70	F	premaxillary	4x2.5	no	uni	no	no	none	asthma	na	yes	immobile
136	802177	19-1461	DD	74	M	Rt parotid	1x1cm	no	uni	no	no	none	k/c/co CA lung	yes	yes	immobile
137	810736	19-1549	S	53	M	submandibular	2x2cm	no	uni	no	no	none	none	na	yes	immobile

S.No	MRD No	Asp No	Radiology	radiology solid /cystic/ complex	Site of FNAC	FNA diag	classification under MSRSGC	Histopathology correlation	Mode of procedure
69	329561	17- 1293	na	na	lt parotid	pleomorphic adenoma	IV benign	-	Direct
70	12568	17-1310	na	na	rt parotid	pleomorphic adenoma	IV benign	-	Direct
71	334522	17-1331	na	na	rt submandibular	cystic lseion SUMP	II	benign epithelial cyst	Direct
72	315836	17-1451	na	na	rt infrauricular	pleomorphic adenoma	IV benign	-	USG guided
73	415326	18-14	na	na	rt parotid	Mucinous lesion	III	Warthins tumor	Direct
74	417353	18-94	na	na	lt submandibular	sialadenosis	II	-	Direct
75	429835	18-132	na	na	rt parotid	pleomorphic adenoma	IV benign	-	Direct
76	434407	18-161	na	na	lt submandibular	chronic sialadenitis	II	-	Direct
77	446821	18-263	na	na	rt parotid	non diagnostic	I	-	Direct
78	451412	18-297	na	na	rt parotid	AUS	III	-	Direct
79	458780	18-384	warthins tumor	solid	lt submandibular	adenoid cyctic carcinoma	VI	Adenoid cystic carcinoma	Direct
80	396413	18-393	na	na	rt parotid	SUMP	IV SUMP	myoepithelioma	Direct
81	472164	18-510	likely warthins tumor	solid	lt parotid	pleomorphic adenoma	IV benign	-	Direct
82	162630	18-580	rt parotid abscess	solid	rt parotid	chronic sialadenitis	II	-	Direct
83	484888	18-649	intensly enhancing lesion	solid	rt parotid	pleomorphic adenoma	IV benign	-	Direct
84	485727	18-659	na	na	lt parotid	pleomorphic adenoma	IV benign	-	Direct
85	494283	18-749	pleomorphic adenom	solid	lt parotid	pleomorphic adenoma	IV benign	-	Direct
86	499475	18-792	cystic mass	cystic	rt parotid	AUS	III	-	Direct
87	505427	18-865	na	na	rt submandibular	chronic sialadenitis	II	-	Direct
88	508534	18-885	na	na	lt parotid	sialadenosis	II	-	Direct
89	515645	18-955	intensely enhancing lesion in b/l parotids	solid	b/l parotids	warthins gtumor	IV benign	warthins tumor	Direct
90	520325	18-991	na	na	soft palate	pleomorphic adenoma	IV benign	pleomorphic adenoma	Direct
91	531446	18-1017	rt submandibular gland inflammation	solid	rt submandibular	chronic sialadenitis	II	-	Direct
92	527329	18-1045	na	na	rt parotid	pleomorphic adenoma	IV benign	pleomorphic adenoma	Direct
93	527488	18-1049	malignant soft tissue involving parotid gland	solid	rt parotid	acute sialadenitis	II	infective pathology	Direct
94	65478	18-1112	well defined hypodense lesion in left parotid	solid	rt parotid	non neoplastic cysts	II	-	Direct
95	539090	18-1172	na	na	rt parotid	pleomorphic adenoma	Iv benign	-	Direct
96	544141	18-1215	lt paroritis with temporomandibular joint abscess	solid	lt sumandibular	granulomatous sialadenitis	II	-	Direct
97	457403	18-1406	pleomorphic adenoma- b/l parotids	solid	lt parotid	SUMP	IV SUMP	-	Direct
98	568810	18-1448	na	na	rt submandibular	AUS	III	warthins tumor	Direct
99	554313	18-1485	plaeomorphic adenoma	solid	rt parotid	pleomorphic adenoma	IV benign	mucoepidermoid carcinoma low grade	Direct
100	572331	18-1535	na	na	lt submandibular	non diagnostic	I	-	Direct
101	583250	18-1580	na	na	lt parotid	warthins tumor	IV benign	warthins tumor	Direct
102	595388	18-1702	na	na	lt cheek	SUMP	IV SUMP	-	Direct
103	390231	18-1716	FDGavid mass in rt parotid	solid	rt parotid	warthins tumor	IV benign	-	Direct
104	596201	18-1718	pleomorphic adenoma	solid	rt parotid	malignant aspirate	VI	?salivary duct carcinoma ? High grade mucoepidermoid carcinoma	Direct
105	606515	18-1795	Mass in deep right parotid	solid	lt parotid	AUS	III	-	Direct
106	660712	19-110	na	na	Left parotid	SUMP	IV SUMP	-	Direct
107	660742	19-143	na	na	Left parotid	non neoplastic cyst	II	-	Direct
108	665396	19- 156	na	na	Right submandibular	AcuteSialadenitis	II	-	Direct
109	667124	19-162	na	na	Left parotid	Warthins tumor	IV benign	-	Direct
110	666849	19- 165	na	na	Right submandibular	Non neoplastic	II	-	Direct
111	671386	19-190	na	na	Left parotid	pleomorphic adenoma	IV benign	spindle cell neoplasm	Direct
112	673397	19-205	na	na	Right submandibular	Nonneoplastic	II	-	Direct
113	675673	19- 226	na	na	Left parotid	pleomorphic adenoma	IV benign	pleomorphic adenoma	Direct
114	675498	19-222	na	na	right parotid	AUS	III	-	Direct
115	676179	19-237	na	na	preauricular	malignant	VI	squamous cell carcinoma	Direct
116	678529	19- 248	na	na	Right submandibular	AUS	III	-	Direct
117	669112	19-278	na	na	lt preauricular	sialadenosis	II	-	Direct
118	720630	19-624	na	na	lt preauricular	warthin tumor	IV bening	Acinic cell carcinoma	Direct
119	723768	19-673	well defined hetrogenously enhancing lesion in superficial lobe of parotid likely beningn	solid	left parotid	Warthins tumor	IV, benign	-	Direct
120	729515	19-733	na	na	Lt submandibular	Chronic sialadenitis	II	Chronic sialaddenitis	Direct
121	437879	19-739	Cystic lesion - Right parotid gland	cystic	Rt parotid	Bening cyctic lesion	II	-	Direct
122	736763	19-804	s/o lymphoma involving salivary glands	solid	Lt parotid	non diagnostic	I	-	Direct
123	727780	19-806	? pleomorphic adenoma	solid	Lt parotid	non neoplastic	II	Warthins tumor	Direct
124	529831	19-847	Bulky Rt parotid gland	solid	rt parotid and submental	squamous cell carcinoma	VI	squamous cell carcinoma	Direct
125	391757	19-915	na	na	Lt submandibular	non neoplastic	II	-	Direct
126	747950	19-930	likely pleomorphic adenoma	solid	rt parotid	pleomorphic adenoma	IV benign	-	Direct
127	748190	19-947	focally enhancing lesion in the rt parotid likely lymphnodes	solid	Rt parotid	chronic sialadenitis	II	-	USG guided
128	750229	19-957	na	na	lt infraauricuar	pleomorphic adenoma	IV benign	-	Direct
129	727580	19-1022	heterogenous texture of lt submandibular gland	solid	-	Chronic sialadenitis	II	-	Direct
130	781104	19-1250	na	na	Infraauricular	AUS	III	-	Direct
131	5020	19-1322	na	na	Right postauricular	suspicoius for malognancy	v	Warthins tumor	Direct
132	784256	19-1326	diffusely enlarged left parotid gland with altered signal	solid	Lt parotid	Chronic sialadenitis	II	-	Direct
133	792798	19-1390	? necrotic lymphnode	solid	lt infraauricuar	AUS	III	Warthins tumor	Direct
134	795621	19-1398	? inflammatory pseudotumor ? Idiopathic caridynia	solid	rt submandibular	nondiagnostic	I	-	Direct
135	332291	19- 1403	na	na	premaxillary	adenoid cystic carcinoma	VI	Adenoid cystic Carcinoma	IHC
136	802177	19-1461	enlarged rt intraparotid lymphnode	solid	rt parotid	s/o warthin	IV benign	-	USG guided
137	810736	19-1549	na	na	rt neck swelling	SUMP	IV SUMP	-	Direct

S.No	MRD No	Asp No	INITIALS	Age	Sex	Site of lesion	Size of lesion	Change in size of lesion	uni / bilateral	Pain	Asso with eating	signs of inflammation	co morbidities	Smoking/ tobacco chewing	well ciecumscribed swelling	mobile / immobile
138	813919	19-1575	HS	46	M	lt parotid	1x1cm	no	uni	no	no	none	none	na	yes	immobile
139	777522	19-1578	OP	71	M	lt submandibular	5x3cm	increasing	uni	no	no	none	alcoholic	yes	yes	immobile
140	793901	19-1677	KK	55	F	lt submandibular	1x1.5cm	no	uni	no	no	none	none	na	yes	immobile
141	838473	19-1760	B	15	M	hard palate	1x1cm	increasing	uni	no	no	none	none	na	yes	immobile
142	396413	19-1902	PK	43	F	submandibular	3x2cm	increasing	uni	no	no	none	none	na	yes	immobile
143	856190	19-1913	GP	25	M	rt submandibular	2x1cm	increasing	uni	no	no	none	none	yes	yes	immobile
144	864672	19-1994	AK	70	F	lt palatal swelling	2x2cm	increasing	uni	no	no	tender	none	na	yes	immobile
145	164694	20-45	HS	50	M	rt parotid swelling	2x2cm	increasing	uni	no	no	none	TB	yes	yes	immobile
146	881558	20-99	IK	36	F	rt submandibular	1x1cm	increasing	uni	present	no	tender	none	na	yes	immobile
147	891560	20-137	VK	50	M	rt parotid	2x1cm	increasing	uni	no	no	none	asthma	na	diffuse	mobile
148	892213	20-143	R	22	F	submandibular	2x1cm& 1.5x1cm	increasing	bilateral	no	no	none	k/c/osjogren syndrome	na	yes	immobile
149	861924	20-	P	13	F	parotid	r1x1& l1x1cm	no	bilateral	no	no	none	none	na	yes	immobile
150	891460	20-180	I	6	M	rt parotid	diffuse	increasing	uni	present	no	none	none	na	yes	immobile
151	900926	20-229	I	27	M	rt parotid	2.8x1.7cm	no	uni	no	no	none	none	na	yes	immobile
152	904691	20-253	AK	53	M	rt parotid swelling	1.5x1cm	increasing	uni	no	no	none	none	yes	yes	immobile
153	894241	20-273	S	48	F	soft palate	1x0.8cm	no	uni	present	no	none	k/c/o adenoid cyctic carcinoma on chemotherapy	na	yes	immobile
154	906755	20-278	DN	67	M	submandibular	1.5x1cm	no	uni	no	no	none	none	na	yes	immobile
155	910896	20-322	AG	58	M	Rt submandibular	1x1cm	increasing	uni	no	no	none	none	na	yes	immobile
156	928284	20-543	MK	54	F	rt parotid	2x2cm	increasing	uni	no	no	none	none	na	yes	immobile
157	437879	20-559	BB	66	M	rt parotid	2x2cm	increasing	uni	no	no	none	none	na	yes	immobile
158	934542	20-635	PK	62	M	Lt parotid	1x1cm	no	uni	no	no	none	none	na	yes	immobile
159	935402	20-648	DJ	20	M	Rt submandibular	1.5x1cm	no	uni	present	exxagerated after eating	none	none	na	yes	immobile
160	781104	20-649	KK	46	F	rt parotid	1x1cm	increasing	uni	no	no	none	none	na	yes	immobile
161	937580	20-681	BD	65	F	Rt submandibular	1.5x1cm	increasing	uni	present	no	none	DM 2	na	yes	immobile

S.No	MRD No	Asp No	Radiology	radiology solid /cystic/ complex	Site of FNAC	FNA diag	classification under MSRSGC	Histopathology correlation	Mode of procedure
138	813919	19-1575	na	na	left parotid	non neoplastic, nonmucinous cyst	I	-	Direct
139	777522	19-1578	likely pleomorphic adenoma	solid	lt angle of mandible	Suspicious of malignancy	v	-	Direct
140	793901	19-1677	na	na	lt submandibular	Chronic sialadenitis	II	Chronic sialaddenitis	Direct
141	838473	19-1760	na	na	hard palate	pleomorphic adenoma	IV benign	pleomorphic adenoma	Direct
142	396413	19-1902	na	na	submandibular swelling	pleomorphic adenoma	IV benign	myoepithelioma	Direct
143	856190	19-1913	na	na	Rt submandibular	AUS	III	-	Direct
144	864672	19-1994	na	na	lt palatal swelling	SUMP	IV SUMP	-	Direct
145	164694	20-45	na	na	rt parotid	pleomorphic adenoma	IV benign	pleomorphic adenoma	Direct
146	881558	20-99	submandibular sialolithiasis with ild acute sialadenitis	solid	-	Chronic sialadenitis	II	-	Direct
147	891560	20-137	cystic lesionsubmandibular gland	cystic	Rt infra auricullar swelling	AUS	III	-	Direct
148	892213	20-143	b/l parotids - bulky	solid	b/l submandibular	granulomatous sialadenitis	II	-	Direct
149	861924	20-	b/l parotids - bulky	solid	b/l parotids	sialadenosis	II	-	Direct
150	891460	20-180	Rt parotitis with suppurative lymphadenitis	solid	rt parotid gland	Acute on chronic sialadenitis	II	-	usg guided
151	900926	20-229	pleomorphic adenoma	solid	rt parotid	AUS	III	hodgkins lymphoma	usg guided
152	904691	20-253	pleomorphic adenoma	solid	rt parotid	SUMP	IV SUMP	-	Direct
153	894241	20-273	biopsy proven case of adenoid cystic carcinoma large heterogenously enhancing lesion in rt maxillary sinus causing destruction of palate, maxillary arch	solid	soft palate	Malignant aspirate	vi	-	Direct
154	906755	20-278	mildly bulky left submandibular gland	solid	lt submandibular	Nonneoplastic	II	-	Direct
155	910896	20-322	na	na	Rt submandibular	chronic sialadenitis	II	-	Direct
156	928284	20-543	na	na	rt parotid	pleomorphic adenoma	IV benign	Pleomorphic adenoma	Direct
157	437879	20-559	na	na	rt parotid	AUS	III	-	Direct
158	934542	20-635	na	na	lt parotid	Non neoplastic	II	-	Direct
159	935402	20-648	na	na	rt submandibular	Acute sialadenitis	II	-	Direct
160	781104	20-649	na	na	rt parotid	non neoplastic cyst	II	-	Direct
161	937580	20-681	na	na	rt submandibular	Acute sialadenitis	II	-	Direct

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Date 9/9/19

The Principal,
DMC, Ludhiana.

Subject: **Approval of Plan of Thesis.**

This is to inform you that the Faculty of Medical Sciences in its meeting held on 29.05.2019 has approved the plan of thesis of **Aastha Sharma**, a student of your college for **MD Pathology** along with the names of Supervisor/Co-Supervisor as under:-

Topic Plan of Thesis

Cytological evaluation of salivary gland lesions with categorization using the Milan reporting system

Supervisor
Dr. Pavneet Kaur Selhi
Prof.,
Dept. of Pathology,
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Co-Supervisor
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Asst. Prof.,
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The student has to submit the four copies of thesis (along with PDF format) , to the Controller of Examinations, BFUHS, Faridkot, at least six months before the commencement of theory examination, if he/she is otherwise eligible to take the examination. He /She must directed to attach a photocopy of this letter with the forwarding letter while submitting thesis to the University along with the letter of approval of University for change of supervisor/Co-Supervisor, change of topic,(if any).

Dr. S P Singh MS(Oph)
Controller of Examinations

Note :

1. *If any discrepancy found regarding topic of thesis or Supervisor/Co-Supervisor, inform undersigned within one month after issue of this letter.*
2. *The student may submit the thesis as per the schedule already conveyed i.e for May/June examination 30th Nov of the preceding the year of examination and for Nov/Dec examinations 31st May of the year of examination.*

CYTOLOGICAL EVALUATION OF SALIVARY GLAND LESIONS WITH CATEGORIZATION USING THE MILAN REPORTING SYSTEM

THESIS PROPOSAL

FOR APPROVAL OF SUBJECT OF THESIS TO BE SUBMITTED IN PARTIAL FULFILMENT OF THE REQUIREMENTS

FOR THE DEGREE OF

MD

In

PATHOLOGY

OF THE

BABA FARID UNIVERSITY OF HEALTH SCIENCES

FARIDKOT

NOVEMBER, 2018

DR. AASTHA SHARMA

DEPARTMENT OF PATHOLOGY
DAYANAND MEDICAL COLLEGE AND HOSPITAL
LUDHIANA

ABSTRACT OF PLAN OF THESIS

Title	CYTOLOGICAL EVALUATION OF SALIVARY GLAND LESIONS WITH CATEGORIZATION USING THE MILAN REPORTING SYSTEM
For the degree of	MD (PATHOLOGY)
Name of the candidate	Dr. Aastha Sharma
Supervisor	Dr. Pavneet Kaur Selhi, Professor, Department of Pathology, DMCH, Ludhiana
Co-supervisor	Dr. Sumit Grover, Assistant Professor, Department of Pathology, DMCH, Ludhiana
Institution	Dayanand Medical College and Hospital, Ludhiana
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Introduction: Salivary gland lesions are a common entity these days. Fine needle aspiration cytology (FNAC) has been increasingly utilized as a minimally invasive procedure for the diagnosis of salivary gland lesions because of their superficial nature and easy accessibility for the procedure.

Aims & Objectives: To study the detailed cytomorphological features of all salivary gland lesion aspirates and classify them according to the Milan system for reporting salivary gland cytopathology. (MSRSGC)

Material & Methods: This study will be conducted in Dayanand Medical College And Hospital, Ludhiana over a period of five years which includes one and half years prospectively and three and a half years retrospectively .All the fine needle aspiration smears from the salivary gland lesions received in the Department of Pathology will be analyzed for cytomorphological features. The lesions will be classified into different categories based on Milan system of salivary gland lesion reporting. Cell blocks will be made whenever sufficient material is available and correlation with histopathology (cell blocks or surgical biopsy specimens) will be done wherever possible.

Clinical Significance: Fine-needle aspiration (FNA) of salivary gland lesions has become widely accepted as an efficient first line diagnostic test and has role to design appropriate management strategies.It can differentiate between neoplastic and non-neoplastic salivary gland lesions, and in cases of a neoplasm, FNA can diagnose many common benign tumors. This will help to guide management.

Keywords: Salivary Gland Lesions, FNAC, Milan system of salivary gland lesion reporting, Clinical & Radiological findings.

(Signature) Candidate	(Signature) Co-Supervisor	(Signature) Supervisor	(Signature) Principal

CERTIFICATE OF FACILITIES AVAILABLE

This is to certify that the facilities for work on the subject of thesis titled **"CYTOLOGICAL EVALUATION OF SALIVARY GLAND LESIONS WITH CATEGORIZATION USING THE MILAN REPORTING SYSTEM"** exist in the Department of Pathology, DMC&H, Ludhiana and will be provided to the candidate. We will see that the data being included in the thesis is genuine and is collected by the candidate herself under our supervision and guidance.

Supervisor

Pavneet

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APPROVAL PROFORMA
BY
RESEARCH & ETHICAL COMMITTEE
DAYANAND MEDICAL COLLEGE & HOSPITAL, LUDHIANA

Name of candidate	Dr. Aastha Sharma
Department	Pathology
Topic of Thesis	CYTOLOGICAL EVALUATION OF SALIVARY GLAND LESIONS WITH CATEGORIZATION USING THE MILAN REPORTING SYSTEM
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Date of enrollment	10th May,2018
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Research Committee

Chairperson
Research Committee

Approved: Yes / ~~No~~

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Ethics Committee

Chairperson
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BABA FARID UNIVERSITY OF HEALTH SCIENCES, FARIDKOT

PROFORMA FOR REGISTRATION OF SUBJECT FOR DISSERTATION

1	NAME OF THE CANDIDATE AND ADDRESS	Dr. Aastha Sharma Dr. Chuni lal memorial hospital, Main Bazar, Tapa, District Barnala. Punjab Pin-148108
2	NAME OF THE INSTITUTE	Dayanand Medical College and Hospital, Ludhiana
3	COURSE OF STUDY AND SUBJECT	MD Pathology
4	DATE OF ADMISSION OF COURSE	10-05-2018
5	TITLE OF THE TOPIC	CYTOLOGICAL EVALUATION OF SALIVARY GLAND LESIONS WITH CATEGORIZATION USING THE MILAN REPORTING SYSTEM

6. BRIEF RESUME OF THE INTENDED WORK

6.1 NEED FOR THE STUDY

Salivary gland neoplasm comprise nearly 6.5% of all the lesions sampled in the head and neck, amongst these, nearly 40% are malignant. Use of ultrasound guidance (USG) and/or magnetic resonance imaging helps inimaging characteristics and the localization of the lesion within the salivary gland . Fine needle aspiration cytology is a highly reliable technique for preoperative diagnosis of salivary gland lesions. It has garnered widespread use and acceptance among clinicians and their patients. Majority of the salivary gland lesions are easily accessible for FNAC either superficially by palpation or by imaging techniques such as USG. Because of the minimally invasive nature of this technique, it is well tolerated by patients without any major complications. It is also a cost effective diagnostic tool with a high sensitivity and specificity of almost 54% to 98%, respectively. It provides prognostic information and sample for ancillary testing such as molecular genetic studies. It provides useful information such as differentiating a neoplastic lesion from a non neoplastic one and further recognizing the lesion is benign or malignant. [1]

Given the wide diversity of tumors arising in the salivary glands, there are many diagnostic challenges within salivary gland cytopathology. Milan system for reporting salivary gland cytopathology is the recent standardized international reporting system for the classification of the salivary gland lesions which categorizes cytology into 6 categories namely:[2]

1. Non diagnostic
2. Non neoplastic

3. Atypia of undetermined significance

4. Neoplastic (Further categorized into Benign and Salivary gland neoplasm of uncertain malignant potential)

5. Suspicious for malignancy

6. Malignant

These categories are designed to reflect the everyday practice of salivary gland cytopathology, maximize communication between cytopathologists and clinicians, and provides estimates of reproducibility and malignancy risk.[3]

6.2 REVIEW OF LITERATURE

The cytology of normal salivary gland consists of acinar cells, ductal epithelial cells and scant fibrovascular stroma.

Acinar cells could be serous or mucinous in nature, appear as regular spherical acini delineated by their basement membrane, held together by small amount of fibrovascular stroma.

Ductal epithelial cells are found as small cohesive sheets or tubules having small cells with dense cytoplasm and round nucleus.

Fine needle aspiration cytology (FNAC) is being employed for preoperative diagnosis of salivary gland lesions for many years. It is a popular method for diagnosis of salivary gland lesions due to their superficial nature and easy accessibility of the procedure.[4]

Given the wide diversity of tumors arising in salivary glands, there are many diagnostic challenges for salivary gland cytopathology one of which is the lack of uniform reporting system.[3] Previous authors have generally attempted to render diagnosis similar to those given by surgical pathologist that reviewed histology, both biopsy or resection specimen.[5] Thus, very precise diagnosis were given in most of the series with attempts made to definitively classify adenomas into categories like pleomorphic, basal cell, myoepithelioma or Warthin while, when only benign salivary gland tissue was seen, the diagnosis was generally as "benign Salivary gland tissue with no pathological change". These challenges were further amplified by the fact that several low grade carcinoma significantly overlap with their benign counterparts.[6,7]

This led a group of experienced cytopathologists and histopathologists to attempt to create a uniform cytological reporting scheme. The proposed

system is based on key principles developed for standardized terminology systems adopted for other body sites like uterine cervix, thyroid, pancreas.[8,9] The standardization effort started in September 2015 at the European Congress of cytology which was held in Milan, Italy under the umbrella of the American Society of Cytopathology (ASC) and the International academy of cytology. Subsequently an international panel of cytopathologists was organized to establish "The Milan System for Reporting Salivary Gland Cytopathology (MSRSGC)."[10]

The Milan system categorizes salivary gland lesions into 6 categories, which are described as follows:

1. Non Diagnostic

This includes cases with: [11]

-Insufficient quantitative and/or qualitative cellular material to make a cytological diagnosis.

-Aspirates with benign elements only, in a setting of clinically or radiologically defined mass

-Nonmucinous cyst contents.

2. Non Neoplastic

This includes specimen lacking evidence of neoplastic process.[12]

Inflammatory metaplastic infective and reactive lesions which includes acute, chronic and granulomatous sialadenitis, sialadenosis, sialolithiasis etc.

A note is added as:

Clinicoradiological correlation is essential to ensure that the specimen is representative of the lesion.

3. Atypia of Undetermined Significance

Salivary gland FNAC that lacks either qualitative or quantitative cytomorphological features to be diagnosed with confidence as non-neoplastic or neoplastic.[13]

In addition, it also includes the FNAC exhibiting an atypical cytomorphologic feature that excludes the possibility of classifying it as "Non-Diagnostic." Most samples will represent reactive atypia or poorly sampled neoplasms.

4. Neoplasm

It is further divided into 2 categories-[14]

a.) Benign neoplasm- Reserved for clear cut benign epithelial and mesenchymal neoplasms such as pleomorphic adenoma, warthin tumor, lipoma, etc.

b.) Salivary gland neoplasm of uncertain malignant potential (SUMP)- reserved for FNAC specimens that are diagnostic of a neoplasm, however, a diagnosis of specific entity cannot be made.

The differential diagnosis includes both benign and malignant tumors.

5. Suspicious For Malignancy

This category includes aspirates which are highly suggestive of malignancy but not definitive. These include high grade carcinomas with limited sampling or other limitation.[15]

6. Malignant

Aspirates which are diagnostic of malignancy. These can be subclassified into Specific type and grades of carcinomas.

Other malignancies such as lymphomas, sarcomas and metastasis are also included in this category.[16]

The categories are designed to reflect the everyday practice of salivary gland cytopathology, maximize communication between cytopathologists and clinicians, provide estimates of reproducibility and malignancy risk.

A study by Ritu Jain et al, included 80 patients who underwent pre-operative FNAC followed by surgical procedure and histologic examination. The histologic diagnosis was considered as the gold standard. FNAC diagnosis was compared with the final histologic impression and concordance assessed. Sensitivity, specificity and diagnostic accuracy of FNAC for malignant lesions were calculated.[17]

Of the 80 cases, majority (67.5%) involved the parotid gland. Eight cases (10%) were non-neoplastic lesions, comprised of sialadenitis, retention cyst and sialadenosis. Of a total of 72 neoplasms, 58 were benign and 14 were malignant salivary gland tumors. A cyto-histologic concordance of benign diagnosis was achieved in 85.7% of cases and for malignant lesions in 92.8% of the malignant tumors. FNAC showed a sensitivity of 92.8%, specificity of 93.9%, a positive predictive value of 81.2% and negative predictive value of 98.4% for malignant salivary gland tumors. There was one false-negative diagnosis and four false-positive cases diagnosed on FNAC. FNAC continues to be a reliable diagnostic technique in hands of an experienced cytopathologist.[17]

S.A. Thiryayi et.al. studied 287 salivary gland aspiration cytology samples received in their department for two years retrospectively and assigned a diagnostic category code from the MSRSGC. Cytology results were correlated with subsequent histology (where available), clinical and radiological follow up.[18]

The specimens were classified as 21.3% non diagnostic, 22% non neoplastic, 2.4% atypia of uncertain significance, 36.9% neoplasm benign, 5.2% neoplasm of uncertain malignant potential, 1.7% suspicious for malignancy and 10.5% malignant (low grade 1.4% and high grade 9.1%) and clinical/radiological follow up was available for 138 (48.1%) specimens, clinical/radiological follow up only for 145 (50.5%) and no follow up for the remaining 4 (1.4%) sample. The risk of malignancy for each category was 8.5% nondiagnostic, 1.6% non neoplastic, 0% atypia of uncertain significance, 1.9% neoplasm benign, 26.7% neoplasm of uncertain malignant potential, 100% suspicious for malignancy and 100% malignant. They found the Milan System for Reporting Salivary Gland Cytopathology as a useful tool to guide clinical management and provide an indication of possible risk of malignancy.[18]

Another retrospective study conducted by Manish Rohilla et. al. over a period of 3 years (2014-2016) evaluated 631 cases. The age of patients ranges from 1 to 95 years with the mean age being 43.7years, male: female ratio was 1.7:1. The parotid gland was the most commonly involved (61.3%) followed by submandibular gland (35.7%) and minor salivary glands (3%). No case of sublingual salivary gland lesion was observed in the study. There were no post FNAC complications in any of these cases.[19]

Non diagnostic aspirations were found to be 2.2% (14 of the 631 cases). Non neoplastic lesions accounted for 55.8% (352 out of 631) whereas 40.4% (225 of 361) were neoplastic. Of the 225 neoplastic lesions 73.7% (188 of 225) were benign and 23.9% (61 of 225) were malignant. 1.6% cases were

classified at cystic lesions and 2.4% cases were classified as neoplasms without further categorizations.[19]

It was concluded from the study that most salivary gland lesions can be accurately diagnosed via FNA sampling. In cases with classic cytomorphological features of a particular neoplasm, a final diagnosis should be preferred to minimize the use of equivocal categories, lead the treating clinician towards an appropriate management strategy and reduce patient anxiety related to indeterminate diagnosis.[19]

A study conducted by Viswanathan K et al on total of 627 salivary gland FNA specimens obtained from 2011 through 2016 were retrieved, with follow-up available for 373 cases. The original diagnoses were recategorized using MSRSGC by 2 independent cytopathologists as: 1) non-diagnostic; 2) non-neoplastic; 3) atypia of undetermined significance (AUS); 4a) benign neoplasms; 4b) salivary gland neoplasm of uncertain malignant potential (SUMP); 5) suspicious for malignancy (SFM); and 6) malignant. The Risk of Malignancy (ROM) and overall ROM for each diagnostic category were determined, with characterization of "indeterminate" (AUS, SUMP, and SFM) lesions.[10]

There was near-perfect agreement regarding categorization (626 of 627 cases; 99.8%) between the 2 cytopathologists, with discordance observed for 1 case. The sensitivity, specificity, negative predictive value, and positive predictive value of salivary gland FNA specimens at the study institution were 79%, 98%, 94%, and 92%, respectively. The ROM for non-diagnostic, non-neoplastic, benign neoplasms, AUS, SUMP, SFM, and malignant were 6.7%,

7.1%, 38.9%, 5.0%, 34.2%, 92.9%, and 92.3%, respectively. The indeterminate category had an overall ROM of 47.1%.[10]

A retrospective study conducted by Layfield LJ on One-hundred and sixty-four cases from a prior cytological study with histological follow-up were re-reviewed by one of the authors and assigned to one of the MSRSGC categories. The original and MSRSCG diagnoses were compared, as were follow-up recommendations.[2]

The MSRSGC system classified 29 specimens as non-diagnostic (seven histologically shown to be benign salivary gland, two non-mucinous cysts, 14 sialadenitis, one pleomorphic adenoma, one haemangioma, one lymphoma, one adenoid cystic carcinoma, one squamous carcinoma and one benign lymphoid proliferation). The original study diagnosed these lesions as: seven benign cysts, 15 benign salivary gland tissue, one benign neoplasm and two insufficient for diagnosis. In seven cases, MSRSGC disagreed with original diagnoses and surgical resection showed lesions where optimal follow-up was more consistent with original cytological diagnosis. In 10 cases with disagreement, the MSRSGC was associated with a more appropriate follow-up based on the surgical diagnosis. Malignancy risks for the Milan categories were: non-diagnostic (12%), non-neoplastic (5%), atypia of undetermined significance (19%), neoplasm, benign (5%), neoplasm (40%), suspicious for malignancy (60%) and malignant (93%). MSRSGC was comparable with the original reported diagnoses in the majority of cases. Both systems had high accuracy for distinguishing benign from malignant lesions and both were associated with appropriate follow-up in most cases.[2]

6.3 AIMS AND OBJECTIVES OF THE STUDY

To study the detailed cytomorphological features of all salivary gland lesions and categorize them according to the Milan system for reporting salivary gland lesions.

7. MATERIALS AND METHODS

7.1 Source of Data

Fine needle aspiration smears from salivary gland lesions received in the Department of Pathology of Dayanand Medical College and Hospital, Ludhiana over a period of one and half years prospective and three and a half years retrospectively (5 year study) will be analysed.

7.2 METHOD OF COLLECTION OF DATA

INCLUSION CRITERIA

FNAC samples from salivary gland lesions received in the cytology lab of the pathology department which would include

1. FNAC samples processed in the department through direct procedure.
2. FNAC slides received in the department after prepaid guided aspiration under ultrasonography and CT guidance.
3. Prepared and stained slides for review from an outside centre.

EXCLUSION CRITERIA-

Samples obtained from lesions other than from salivary gland origin.

PROCEDURE

After informed consent, fine needle aspiration (FNAC) will be done using 21 guage needle for salivary gland lesions attached to 20cc disposable plastic syringe .Taking aseptic precautions, needle will be introduced into the lesion/swelling slides will be prepared immediately. One of the slide will be utilized for rapid on site evaluation for adequacy by staining with Toulidine Blue stain. Two of them will be wet fixed in 95% ethanol and stained with Papanicolaou stain and Hematoxylin and Eosin .The remaining smears will be air dried and stained by May Grunwald Giemsa stain.

DURATION OF STUDY

Five year study of which one and half year will be prospective study and three and a half years will be retrospective study.

OUTCOME

The smears obtained by FNA of all salivary gland lesions will be analysed in this study and will be categorized according to the Milan system of reporting salivary gland lesions. The cytological findings will be correlated with the clinico-radiological profile, cell block findings, histopathological findings, special stains and IHC findings wherever possible.

STATISTICAL ANALYSIS

Data will be described in terms of range; mean ±standard deviation (± SD), median, frequencies (number of cases) and relative frequencies (percentages) as appropriate. All statistical calculations will be done using SPSS (Statistical Package for the Social Science) SPSS 21 version statistical program for Microsoft Windows.

7.3 DOES THE STUDY REQUIRE ANY INVESTIGATIONS OR INTERVENTIONS TO BE CONDUCTED ON PATIENTS OR OTHER HUMANS OR ANIMALS? IF SO, PLEASE DESCRIBE BRIEFLY.

Not Applicable

7.4 HAS ETHICAL CLEARANCE BEEN OBTAINED FROM YOUR INSTITUTION IN CASE OF 7.3?

Yes

8. LIST OF REFERENCES

1. Seethala RR, Li Volsi VA, Baloch ZW. Relative accuracy of fine-needle aspiration and frozen section in the diagnosis of lesions of the parotid gland. Head Neck. 2005;27(3):217-23.
2. Layfield LJ, Baloch ZW, Hirschowitz SL, Rossi ED. Impact on clinical follow-up of the Milan System for salivary gland cytology: A comparison with a traditional diagnostic classification. Cytopathology. 2018;29(4):335-42.
3. Solomon D, Davey D, Kurman R, Moriarty A, O'Connor D, Prey M, et al. The 2001 Bethesda System: terminology for reporting results of cervical cytology. JAMA. 2002;287(16):2114-9.
4. Daneshbod Y, Daneshbod K, Khademi B. Diagnostic difficulties in the interpretation of fine needle aspirate samples in salivary lesions: Diagnostic pitfalls revisited. Acta Cytol. 2009;53:53-70.
5. Kline TS, Merriam JM, Shapshay SM. Aspiration biopsy cytology of the salivary gland. Am J Clin Pathol.1981;76(3):263-9.
6. Rossi ED, Wong LQ, Bizzarro T, Petrone G, Mule A, Fadda G, et al. The impact of FNAC in the management of salivary gland lesions: Institutional experiences leading to a risk based classification scheme. Cancer Cytopathol. 2016;124:388-96.
7. Rossi ED, Faquin WC, Baloch Z, Barkan GA, Foschini MP, Pusztaszeri M, et al. The Milan System for Reporting Salivary Gland Cytopathology: Analysis and suggestions of initial survey. Cancer. 2017;125(10):757-66.

8. Nayar R, Wilbur DC. The Pap test and Bethesda 2014. Cancer Cytopathol. 2015;123-271-81.
9. Ali SZ, Cibas E, eds. The Bethesda System for Reporting Thyroid Cytopathology: Definitions, Criteria and Explanatory Notes. 1st ed. New York: Springer US; 2010.
10. Viswanathan K, Sung S, Scognamiglio T, Yang GCH, Siddiqui MT, Rao RA. The role of the Milan System for Reporting Salivary Gland Cytopathology: A 5-year institutional experience. Cancer Cytopathol. 2018;126(8):541-51.
11. Foschini MP, Rossi ED, Higuchi K, Jhala NC, Kholová I, Urano M, et al. Non-Diagnostic. Faquin WC, Rossi ED, Baloch Z, Barkan GA, Foschini MP, Kurtycz DFI (editor). The Milan system for reporting Salivary Gland cytopathology. Switzerland: Springer; 2018. pp. 11-20.
12. Faquin WC,, Bongiovanni M, Callegari FM, Canberk S, Elsheikh TM, Kurtycz DFI et al. Non-Neoplastic. Faquin WC, Rossi ED, Baloch Z, Barkan GA, Foschini MP, Kurtycz DFI (editor). The Milan system for reporting Salivary Gland cytopathology. Switzerland: Springer; 2018. pp. 21-42.
13. Pusztaszeri M, Baloch Z, Faquin WC, Rossi ED, Tabatabai ZL. Atypia of Undetermined Significance. Faquin WC, Rossi ED, Baloch Z, Barkan GA, Foschini MP, Kurtycz DFI (editor). The Milan system for reporting Salivary Gland cytopathology. Switzerland: Springer; 2018. pp. 43-54.
14. Baloch Z, Fadda G, Fırat P, Klijanienko J, Krane JF, Layfield L, et al. Neoplasm. Faquin WC, Rossi ED, Baloch Z, Barkan GA, Foschini MP,

Kurtycz DFI (editor). The Milan system for reporting Salivary Gland cytopathology. Switzerland: Springer; 2018. pp. 55-84.

15. Rossi ED, Field AS, Ali SZ, Chandra A, Gong Y, Maleki Z, et al. Suspicious for Malignancy. Faquin WC, Rossi ED, Baloch Z, Barkan GA, Foschini MP, Kurtycz DFI (editor). The Milan system for reporting Salivary Gland cytopathology. Switzerland: Springer; 2018. pp. 85-96.
16. Mehrotra S, Al-Abbadi MA, Barkan GA, Pambuccian SE, Vielh P, Wang H, et al. Malignant. Faquin WC, Rossi ED, Baloch Z, Barkan GA, Foschini MP, Kurtycz DFI (editor). The Milan system for reporting Salivary Gland cytopathology. Switzerland: Springer; 2018. pp. 97-139.
17. Jain R, Gupta R, Kudesia M, Singh S. Fine needle aspiration cytology in diagnosis of salivary gland lesions: A study with histologic comparison. Cytojournal. 2013;10:5.
18. Thiryayi SA, Low YX, Shelton D, Narine N, Slater D, Rana DN. A retrospective 3-year study of salivary gland FNAC with categorisation using the Milan reporting system. Cytopathology. 2018;29(4):343-8.
19. Rohilla M, Singh P, Rajwanshi A, Gupta N, Srinivasan R, Dey P, et al. Three-year cytohistological correlation of salivary gland FNA cytology at a tertiary center with the application of the Milan system for risk stratification. Cancer Cytopathol. 2017;125(10):767-75.

PROFORMA

Serial no.- **Asp. No**

Name **Age** **Sex**

MRD No. **Date-**

Address **Phone No:**

Clinical features

Site of lesion Size of the lesion

Change in size of lesion Unilateral/Bilateral:

Pain

Association with eating

Signs of inflammation- warmth/tenderness/overlying skin/ lymphadenopathy

Co morbidities-

Past History-

History of smoking-

Clinical Examination-

Radiological Findings-

Signature of Candidate **Signature of Supervisor**

Followup-

Site of FNAC-

FNA Findings-

Classification of the lesion under MSRSGC –

Histopathological Findings (Cell block/ Biopsy)-

Signature of Candidate

Signature of Supervisor